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THE EFFECT OF PITRESSIN AND WATER INTAKE ON THE CEREBROSPINAL FLUID

BY

J. N. CUMINGS AND N. S. ALCOCK

From the National Hospital, Queen Square, London

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FREMONT SMITH *et alia* (1930) have shown that dilution of the blood and of the cerebrospinal fluid (C.S.F.) occurs on giving subjects large quantities of water by mouth after a preliminary subcutaneous injection of extract of the posterior lobe of the pituitary (vasopressin). In their experiments sodium, chlorides, protein, non-protein nitrogen, total solids, and freezing-point estimations were made. The few figures shown do not suggest an even alteration of blood and C.S.F. In a later paper (1931) they again measured the depression of the freezing-point of blood and C.S.F. in patients subjected to similar experiments as before. They showed in these later experiments that in seven out of nine cases depression of the freezing-point of both blood and C.S.F. occurred, but in two cases there was an elevation of the freezing-point of the C.S.F. with a lowering of that of the blood.

We have conducted experiments of a similar character, but have estimated different constituents of the blood and C.S.F. Our results and the interpretation of these are recorded below.

Methods

After blood and C.S.F. had been obtained from patients who had, with only the few exceptions stated in the tables, fasted for some hours, 0·5 c.c. of pitressin was administered subcutaneously. During the next 4 hours 6 pints of water were drunk, as large a quantity as possible being taken within the first 2 hours. At the end of the 4 hours blood and C.S.F. were again withdrawn.

There were four groups of male patients. The first consisted of seven normal subjects from whom lumbar C.S.F. was obtained ; the second of two subjects from whom ventricular fluid was taken, the third of patients who had spinal lesions producing a spinal block and from whom C.S.F. from below the block was withdrawn ; and, lastly, a group of two subjects from whom hydrocele fluid and blood were taken for examination.

The following constituents in these fluids were estimated : hæmoglobin, blood only, by Haldane's method ; sugar by Folin and Wu's method ; urea by Archer's modification of Folin and Wu's method ; calcium by Kramer and Tisdall's method ; inorganic phosphorus by Brigg's method (Harrison, 1937) ; magnesium and chlorides (McCance and Shipp, 1933). Duplicate samples in every case of all four specimens (two of blood and two of C.S.F.) were estimated together for each of these substances. If any variation occurred between the duplicates, further samples were estimated.

Results

The full list of results in all 14 cases is recorded at the end of the paper. There was a gain in weight in the patients which, in every case, corresponded with the weight of water drunk, when the weight of the urine passed was taken into consideration. The amount of urine passed in most cases was not more than a few fluid ounces.

In general the blood diluted in every case ; however, the individual constituents did not dilute evenly. The C.S.F. behaved differently in the different groups of patients. In group I (lumbar fluid from normal patients) there was not only an irregular dilution of the C.S.F. but in certain instances some of the constituents increased in concentration. For example, urea increased in subjects S and L, calcium in subject S, phosphorus in subject M, magnesium in subject L, and chlorides in subjects K and S. This was also true for group II (ventricular fluid), and the similarity of these results suggests that changes found in the lumbar C.S.F. may be taken as a true reflection of the changes taking place in the ventricular fluid. It is seen that in group III (lumbar fluid from below a spinal block) there is much less dilution of the C.S.F. and in many instances there is practically none at all. Group IV (those from whom hydrocele fluid was examined) shows that hydrocele fluid diluted in every instance, and as will be seen later, in a very similar ratio to the dilution occurring in the blood.

If the Donnan theory for the formation of the C.S.F. were true, the ratio of the concentration of the same substance in the C.S.F. to that in the blood should remain the same before and after dilution, or at least the variation between the ratios should be slight. Further, if in one subject the ratio for one substance did vary, then the ratios for the other substances should vary in a corresponding manner. Accordingly the results have been expressed in terms of this ratio in the following tables.

GROUP I

Results expressed as the ratio $\frac{\text{concentration of substance in blood}}{\text{concentration of substance in lumbar C.S.F.}}$

NAME		SUGAR	UREA	CALCIUM	INORGANIC PHOSPHORUS	MAGNESIUM	CHLORIDES
*H	Before experiment.	1·24	1·14	1·66	1·05	0·74	0·84
	After dilution.	1·37	0·94	1·72	1·09	0·72	0·77
M	Before experiment.	1·46	1·10	1·80	1·15	0·80	0·82
	After dilution.	1·42	0·98	1·90	1·08	0·82	0·79
K	Before experiment.	1·20	1·16	2·17	1·09	0·82	0·83
	After dilution.	1·10	1·20	2·27	1·08	0·78	0·80
A	Before experiment.	1·14	1·03	2·10	1·90	0·69	0·79
	After dilution.	1·09	1·02	2·08	1·90	0·61	0·74
*B	Before experiment.	—	0·93	1·60	1·45	0·79	0·83
	After dilution.	—	0·94	1·57	1·25	0·75	0·74
L	Before experiment.	1·30	1·26	1·74	1·87	1·14	0·82
	After dilution.	1·29	1·09	1·78	1·83	1·00	0·82
S	Before experiment.	1·30	1·08	1·90	1·60	—	0·84
	After dilution.	1·15	0·83	1·86	1·60	—	0·77

GROUP II

Results expressed as the ratio $\frac{\text{concentration in blood}}{\text{concentration in ventricular C.S.F.}}$

NAME		SUGAR	UREA	CALCIUM	INORGANIC PHOSPHORUS	MAGNESIUM	CHLORIDES
S	Before experiment.	1·20	1·40	2·70	2·00	0·72	0·81
	After dilution.	1·15	1·08	3·00	1·86	0·68	0·70
K	Before experiment.	1·34	1·10	2·30	1·04	0·70	0·80
	After dilution.	1·30	1·14	1·99	1·02	0·70	0·79

GROUP III

Results expressed as the ratio $\frac{\text{concentration in blood}}{\text{concentration in lumbar C.S.F. below block.}}$

NAME		SUGAR	UREA	CALCIUM	INORGANIC PHOSPHORUS	MAGNESIUM	CHLORIDES
A	Before experiment.	1·30	1·03	1·75	1·55	0·63	0·86
	After dilution.	1·28	0·89	1·70	1·40	0·68	0·78
R	Before experiment.	1·50	1·10	2·08	1·50	1·03	0·79
	After dilution.	1·20	1·09	1·90	1·30	0·87	0·76
B	Before experiment.	1·90	1·00	2·10	1·04	0·94	0·84
	After dilution.	1·60	0·91	2·10	1·10	0·97	0·74

GROUP IV

Results expressed as the ratio $\frac{\text{concentration in blood}}{\text{concentration in hydrocele fluid.}}$

NAME		SUGAR	UREA	CALCIUM	INORGANIC PHOSPHORUS	MAGNESIUM	CHLORIDES
*H	Before experiment.	0·70	1·09	1·06	1·15	0·97	0·94
	After dilution.	0·77	0·96	1·04	1·17	0·94	0·83
*E	Before experiment.	—	0·95	1·24	1·20	1·19	0·92
	After dilution.	—	0·96	1·30	1·09	1·13	0·88

* Not fasting.

Discussion

It will be seen from these figures that the ratio of blood to hydrocele fluid after dilution of the blood has not appreciably altered. In fact, the constituents of these two fluids have followed each other very closely. The dilution of hydrocele fluid being so regular and retaining so constant a ratio to the blood points to this dilution being the result of dialysis. It may also be assumed that the rate of blood dilution is fairly regular and that other fluids, such as C.S.F., should dilute in a manner similar to hydrocele fluid if the mechanism for their dilution be the same. When consideration is given to the other tables it is seen that the C.S.F. from below a spinal block shows a marked contrast to the hydrocele fluid in that there is a very considerable variation in the ratio before and after dilution. In nearly half of the various substances estimated there is a variation of more than 10 per cent. between the two ratios. An inspection of the tables giving the actual amounts of each substance present shows that this variation in the ratios before and after dilution is due to the fact that the C.S.F. has been only very slightly diluted. This suggests that the spinal subarachnoid space is not similar to any serous surface, in that the alteration of substances across the membranes is not controlled according to the theory of dialysis.

It is possible to consider groups I and II together. In both there is an irregular variation in the ratios, about one-third varying by more than 10 per cent. As examples of this variation the following may be quoted: urea in subject H, phosphorus and chlorides in subject B, urea and magnesium in subject L, sugar and urea in subject S, and calcium in subject K. In each of these specific cases the C.S.F. has diluted less than the blood. If there was any lag, due to the time factor, in the balancing mechanism between blood and C.S.F. in these experiments, then all constituents of the C.S.F. should be equally affected. Thus, if one ratio varied by as much as 10 per cent., then the ratio for the other constituents should have varied similarly. This would be the case if the assumption were true that dialysis was the only mechanism involved. Further, if in these experiments water only passes from the blood to dilute the C.S.F. there should be relatively little lag. It has also been shown that in the case of hydrocele fluid there is no such lag at the end of 4 hours. It is not reasonable to suggest that tissue fluid from the perivascular spaces plays any part as there was no increase of cells between the two C.S.F. specimens taken before and after dilution. It is difficult to believe that fluid from the perivascular spaces should pass into the C.S.F. without a certain number of cells coming into it and being found in the C.S.F.

It is possible that pitressin may act on the choroid plexus and so account for the irregularity of dilution. Pitressin has been shown to act on glandular organs (Dodds and Noble (1937), Dodds (1937)), but the choroid plexus is not morphologically similar to other glandular structures. If, however, pitressin does affect the choroid plexus, the theory that the C.S.F. is formed across a passive dialysing membrane is difficult to uphold.

The results appear to be capable of explanation if it be admitted that the choroid plexus takes an active part in the control of the C.S.F. formation and that following dilution of the blood the choroid plexus either by a secretory

process or by means of selective filtration lets through substances in varying concentrations. However, there is another possibility that has to be considered. As well as some activity on the part of the choroid plexus, it is possible that absorption of individual constituents takes place in the C.S.F. If this were so it would appear that the rate of absorption varies not only from one constituent to another, but also that the same constituent is absorbed at different rates by different individuals. It is only possible to explain the variation of the ratios on such an assumption. In view of the results recorded here the assumption of Fremont-Smith that the alteration of the freezing-point in his experiments was evidence of dialysis in the formation of the C.S.F. would not be correct. Therefore from our experimental results recorded in this paper it must be assumed that either the choroid plexus performs an active function in the production of the C.S.F., or that the varying rate and selectivity of absorption is responsible, or, and this is more probable, that both are concerned. The rate of absorption may also be an individual characteristic. If the choroid plexus is accepted as playing an active part in the formation of the C.S.F. as in one suggestion from the above, then support is given to the contention of Flexner (1934), who showed that a definite amount of energy (13 calories) was produced during the formation of 1 litre of C.S.F. He stated that the C.S.F. could not be a dialysate nor could it be an ultrafiltrate, because ultrafiltration would only account for 0·9 calories. He therefore maintained that the C.S.F. was a secretion, using this in the sense that work was done during its formation and not in the sense that the choroid plexus was a glandular structure.

Summary

Investigations have been conducted by which the blood has been diluted and the behaviour of the C.S.F. in relation to this has been subsequently studied.

It has been found that the C.S.F., both ventricular and lumbar, does not dilute equally with the blood in such constituents as have been examined. Hydrocele fluid, however, does follow blood dilution closely.

C.S.F. from below a spinal block shows extremely little dilution.

These findings have been discussed in relation to the mechanism for the formation and absorption of the C.S.F.

It is with pleasure that we acknowledge our gratitude to the members of the Staff of the National Hospital for permission to study patients under their care ; to Mr. W. H. Henderson, F.R.C.S., for his help with the ventricular punctures ; and to Mr. Nunn for technical assistance.

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GROUP I. Normal subjects from whom *lumbar C.S.F.* was withdrawn.

NAME	TIME, IN HOURS	SUGAR		UREA		CALCIUM		INORGANIC PHOSPHORUS		MAGNESIUM		CHLORIDES		HÆMOGLOBIN
		BLOOD	C.S.F.	BLOOD	C.S.F.	BLOOD	C.S.F.	BLOOD	C.S.F.	BLOOD	C.S.F.	BLOOD	C.S.F.	BLOOD
*H	0	64·5	52·0	31·5	27·5	10·0	6·0	4·75	4·5	2·46	3·41	616·6	736·4	111
	4	64·5	46·5	23·5	25·0	9·7	5·6	4·65	4·25	2·36	3·28	531·6	674·4	101
M	0	87·0	59·5	28·0	24·75	10·0	5·4	2·53	2·12	2·27	2·82	598·04	723·0	120
	4	84·5	59·5	20·75	21·5	9·8	5·1	2·40	2·225	2·21	2·7	552·2	698·5	113
K	0	67·0	55·7	25·5	22·0	10·2	4·66	4·21	3·87	4·3	5·24	554·6	659·88	105
	4	60·0	55·0	22·5	18·5	10·0	4·4	4·0	3·7	3·91	5·01	530·5	662·2	94
A	0	74·0	64·5	46·5	45·0	11·0	5·2	5·1	2·58	2·4	3·48	599·0	750·0	—
	4	65·0	59·0	45·0	44·0	10·4	5·0	4·9	2·54	2·12	3·45	526·5	706·7	—
*B	0	—	65·0	26·5	28·5	12·0	7·5	2·9	2·0	3·85	4·85	575·0	688·5	106
	4	—	60·0	25·0	26·5	10·7	6·8	2·5	2·0	3·45	4·6	480·2	650·8	102
L	0	72·0	55·5	19·0	15·0	12·4	7·1	4·6	2·45	4·9	4·3	603·7	738·3	105
	4	61·0	48·5	17·0	15·5	11·6	6·5	4·16	2·28	4·4	4·42	575·6	716·0	100
S	0	78·0	61·0	31·5	29·0	10·9	5·7	2·75	1·8	—	—	606·1	719·5	107
	4	70·0	61·0	24·5	29·25	10·7	5·8	2·6	1·6	—	—	563·9	725·4	101

GROUP II. Normal subjects from whom *ventricular C.S.F.* was withdrawn.

S	0	61·0	51·0	21·3	15·0	11·2	4·1	3·37	1·64	2·89	4·03	570·9	699·7	105
	4	54·0	47·0	15·5	14·7	10·8	3·6	2·68	1·44	2·62	3·81	468·0	664·56	102
K	0	65·0	48·5	25·0	22·5	10·6	5·0	3·5	3·34	2·71	3·9	542·9	678·6	109
	4	63·0	48·0	23·5	20·5	10·1	5·1	3·0	2·94	2·52	3·29	508·4	641·7	100

All results are expressed in mgms. per cent.
* Not fasting.

GROUP III. Subjects with a spinal block from whom *lumbar C.S.F.* was withdrawn *below the block*.

NAME	TIME IN HOURS	SUGAR		UREA		CALCIUM		INORGANIC PHOSPHORUS		MAGNESIUM		CHLORIDES		HÆMO-GLOBIN
		BLOOD	C.S.F.	BLOOD	C.S.F.	BLOOD	C.S.F.	BLOOD	C.S.F.	BLOOD	C.S.F.	BLOOD	C.S.F.	BLOOD
A	0	89·0	67·0	29·9	29·0	9·8	5·6	3·87	2·5	2·8	4·4	601·4	699·7	104
	4	87·0	68·0	26·7	30·0	9·1	5·4	3·37	2·37	2·73	4·0	547·6	697·3	93
R	0	68·0	46·2	19·7	18·0	10·4	5·0	4·5	3·0	3·29	3·2	578·0	730·1	99
	4	61·0	46·5	18·5	17·0	9·4	5·0	4·03	3·0	2·92	3·32	551·1	725·4	95
B	0	122·0	62·5	25·7	25·5	10·1	4·8	1·53	1·47	3·08	3·28	594·4	704·3	88
	4	98·0	61·5	21·2	23·5	10·0	4·7	1·35	1·18	2·87	2·96	526·5	706·7	79

Subjects A and R both had a complete spinal block, but that of subject B was only partial.

GROUP IV. Subjects from whom *hydrocele fluid* was withdrawn.

*H	0	64·5	92·0	31·5	29·2	10·0	9·4	4·75	4·13	2·46	2·52	616·6	650·3	111
	4	64·5	83·0	23·5	24·7	9·7	9·3	4·65	3·95	2·36	2·49	531·6	643·5	101
*E	0	—	—	19·0	19·9	11·9	9·6	3·22	2·7	2·54	2·13	552·2	599·0	101
	4	—	—	16·3	16·7	11·7	9·0	2·84	2·6	2·17	1·91	512·4	574·5	89

All results expressed in mgms. per cent.

* Not fasting.

PSEUDOHERMAPHRODITISM, ADIPOSITY, POLYURIA, AND HYPERGLYCÆMIA. AN INFUNDIBULO-TUBERIAN SYNDROME

BY

R. M. STEWART

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ALTHOUGH the literature contains numerous reports of adiposo-genital dystrophy, the number of cases in which it has been possible to investigate the tissues after death is comparatively small. For this reason, it may be of some interest to place on record the clinical history of an instance of this kind, together with the results of a complete post-mortem examination, including the microscopic investigation of the central nervous system.

Case Report

M.C., a boy aged 16 years, was admitted to the Leavesden Hospital on 4th May, 1932. His mother was an unmarried Swiss girl who came to this country in her twenty-fifth year. Nothing was known of the father save that he was of the same nationality. The patient was born in Queen Charlotte's Hospital on 18th June, 1915, and remained in the care of his mother until her return to Switzerland in 1920 ; subsequently a great-aunt took charge of the defective until his admission to hospital. During pregnancy the mother enjoyed good health, but is said to have resorted to tight-lacing in order to conceal her condition. Born at term, the child was of normal proportions and was breast fed for a year. He was a feeble infant, neglected and undernourished. At the end of twelve months he could neither stand nor walk, and he made no attempt to speak until he was eighteen months old. Signs indicating mental deficiency were noted at an early age ; by his third year he had learnt to walk, but the ordinary language of infancy was not acquired until two years later. Habits of cleanliness were not established until his twelfth year. He learnt to dress himself, but always required assistance in washing. When six years old he was rejected as not educable at an ordinary elementary school, and subsequent efforts to teach him to read and write by private tuition proved fruitless. In his early years he enjoyed good health and was described as being a lively and sociable child.

The genital defect was noted at birth, but obesity was not a noticeable feature until his third year. The increase in weight was progressive and when five years old his appearance was grotesque, the excessive obesity and the dwarfism making him " as broad as he was long." At this age, too, a new symptom, excessive thirst, developed, and he drank enormous quantities of milk, water, and eau sucré. Micturition became correspondingly frequent, and in the words of his foster-mother " one saw him nearly always in this action."

In 1925, when he was nine years of age, he began to show marked somnolence,

which gradually increased until ultimately it became so pronounced that he went to sleep as soon as he sat down, no matter what hour of the day. It was this symptom and his excessive obesity for which advice was sought at the French Hospital in 1926. On examination in this hospital on 30th January, 1926, he was noted to show generalized adiposity, his weight being 9 st. 3 lb. and his height 4 ft. 2 in. The tissues were firm, well coloured and the abdomen protuberant. The penis and scrotum were very small and hidden in folds of fat, giving at first glance the impression of female organs. Umbilicus-soles measurement, 65 cm. ; umbilicus-vertex, 69 cm. Micturition was frequent and urgent and he had little control over the movement of his bowels. Mentally he was alert when moving about, but was overcome by sleep as soon as he sat down. He understood simple phrases and repeated spoken words in a low voice but with faulty articulation. He could neither read nor count, but recognized his friends, for whom he showed affection. When asleep in bed he snored loudly and became a little cyanosed. The clinical notes do not refer to the urinary output, but the urine was noted to be free from sugar and there was no glycosuria after the oral administration of 80 gm. of glucose. A second examination made fifteen days later still showed an absence of sugar, but the urine now contained albumen, 0·4 gm. per litre. The patient remained in hospital for four weeks and on nineteen occasions an evening rise of temperature to 99° F. was recorded ; the pulse rate varied between 80 and 92.

Re-examined on 18th February, 1929, the patient was noted to have gained 2 in. in height and to be 1 st. lighter in weight. The skin was smooth, the hair on the scalp abundant, the muscles hypotonic, and the genital organs undeveloped and showing the features of external hermaphroditism. The systolic blood pressure was 98 and the diastolic 58 mm. Hg. Marked polydipsia and polyuria were present. Blood : red blood corpuscles, 4,600,000 ; white blood corpuscles, 9,000 ; hæmoglobin, 86 per cent. Colour index, 0·9. Polymorphs, 4,860 ; eosinophils, 0 ; basophils, 180 ; lymphocytes, 3,600 ; monocytes, 360. The blood Wassermann reaction was negative. The specific gravity of the urine was 1,025, and sugar was present, but no acetone bodies, nor albumen. The fasting blood sugar was 135 mg. per cent. After ingestion of glucose the following curve was obtained : ½ hr., 181 mg. ; 1 hr., 287 mg. ; 1½ hrs., 225 mg. ; 2 hrs., 129 mg. per cent. X-ray examination of the skull showed a pituitary fossa much smaller than normal.

He was admitted to hospital on 4th May, 1932, when the following observations were made.

The patient was an imbecile boy, aged 16½ years ; height 4 ft. 5 in., weight 8 stone 6¾ lb. Circumference of head, 52·7 cm.; breadth, 14·9 cm.; length, 18·1 cm.; cephalic index, 83. He was remarkably stunted in growth, with a brachycephalic head, long face, short, thick neck, and rather slender limbs. His appearance was that of a eunuchoid with pronounced feminine characteristics (Fig. 2). On the scalp there was an abundant growth of dark curly hair, but on the face there were only fine lanugo hairs ; the axillæ were hairless. The skin, smooth, soft, and velvety, was of a reddish hue on the face and pale elsewhere. The face was large, the eyes rather close together, the nose long and straight, the cheeks fat, the lower jaw large and with a slight double chin. The upper teeth were crowded together, the palate high, the tonsils enlarged, and the tongue dry and coated. The pomum adami was not visible on the short, fat neck. The voice was high-pitched and feminine in character. The contour of the body was most unusual, the shoulders being broad and square, the thorax wide, and the abdominal wall covered with a heavy mantle of fat which dragged the skin downwards so that it hung in a heavy apron concealing the pubes and upper thirds of his thighs. There was slight development of the breasts, and, as may be seen from the accompanying illustration, the weight of subcutaneous fat had displaced downwards the nipples and umbilicus. The upper limbs were slender, feminine in contour, and the hands relatively small. The lower limbs were also somewhat slender and free from excess of subcutaneous tissue. There was considerable deformity and eversion of the

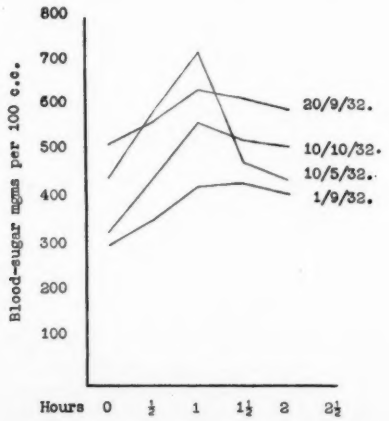
left leg, due partly to an old-standing fracture at the hip joint and partly to a chronic enlargement of the knee-joint. There was a moderate degree of genu valgum and pes planus. The feet and toes were broad. The symphysis-vertex measurement exceeded the symphysis-soles height by 3 in.

There was a well-marked mons veneris covered with thick hair of feminine distribution. The penis measured 2 cm. from symphysis to meatus and had a fully formed glans. About 3·5 cm. behind the penis there was a small rounded eminence with a centrally placed orifice which admitted the tip of the little finger. A nodule the size of a small bean which was felt lying deeply behind the eminence was probably a testicle ; the other testicle could not be felt. Examination of the thoracic and abdominal viscera revealed no abnormality.

X-ray films of the cranium showed bones of normal density with normal coronal and lambdoid sutures ; the sella turcica was, however, small. The bones of the forearms and hands were rather long and slender and the terminal phalanges pointed with feebly developed tufts. The arrangement of the epiphysis of the radius, ulna, and bones of the hand was normal and all were ununited. There was a deformity at the upper end of the left femur owing to the presence of an old fracture through its neck. The subpubic angle was wide, resembling that of a female pelvis.

The patient was a low-grade imbecile, his mental age, estimated by Burt's modification of the Binet-Simon scale, being two and a half years. He was shy, retiring, stubborn, and at times destructive. All his actions were slowly performed and he needed encouragement before he would answer questions. He knew no letters of the alphabet, but could give his name. He fed and dressed himself but needed assistance in washing. At times he was faulty in habits. He was quite alert and showed no drowsiness or tendency to fall asleep during the daytime. He asked frequently for drinks.

Blood examination gave the following : Hæmoglobin, 100 per cent. Red blood corpuscles, 5,300,000. Colour index, 0·94. White blood corpuscles, 12,400. Polymorphs, 7,320. Eosinophils, 125. Lymphocytes, 4,210. Monocytes, 745. He passed large quantities of pale urine. An attempt was made to estimate the fluid intake and the output volume of urine, but owing to his habits and lack of co-operation no accurate figures could be obtained. Over a period of eight days the patient's daily excretion of urine varied between 1,900 c.c. and 3,200 c.c., the average excretion in 24 hours being 2,330 c.c. The urine contained 540 mg. of sugar per 100 c.c. Blood sugar curves after the oral administration of 50 gm. glucose yielded the following graphs.



The cerebrospinal fluid was examined on 17th September, 1932. It contained 240 mg. of sugar per 100 c.c. ; no other abnormality was present.

The patient was put on an ordinary mince diet, which included bread and milk, and no medicinal treatment was prescribed. He continued to drink large quantities of water and on one occasion when he could not get access to a tap was found drinking the contents of a urine bottle. He remained active and alert with no evidence of drowsiness until 2nd February, 1933, when he developed a quinsy. His temperature rose to 103° F. and five days later he succumbed to broncho-pneumonia.

Pathological Findings

A necropsy was carried out 20 hours after death. The body, which was extremely obese, showed a deposit of fat 1 in. in thickness on the anterior abdominal wall. The mammæ were represented by discs of areolar tissue and fat 2½ in. in diameter. A small left testicle (weight 3 grm.) was found lying in the tissues behind the perineal eminence ; the latter appeared to be a rudimentary scrotum and the small orifice seen on it proved to be nothing more than a rather marked dimpling or infolding of its cutaneous surface ; the right testicle (weight 2·40 grm.) lay in the inguinal canal.

The brain weighed 1,380 grm. ; there was slight thickening of the pia arachnoid of the frontal poles ; and the convolutions were large and simple. The base of brain was normal, there being no evidence of tumour or meningitis ; the infundibulum and tuber cinereum were rather small in proportion to the rest of the brain. The pituitary gland was rather small, especially its anterior lobe ; it weighed 0·40 grm. The thyroid and parathyroid glands were normal in appearance. A large thymus gland was present. Both lungs showed a condition of broncho-pneumonia. The heart was normal in size and weighed 270 grm. The myocardium was soft and slightly fatty ; the valves were normal. The large arteries were hypoplastic. The liver, weighing 1,590 grm., was moderately enlarged, congested, and slightly fatty. The kidneys weighed : the right, 1,259 grm., and the left, 1,309 grm. Fœtal lobulation present, otherwise there was no abnormality. The pancreas weighed 65 grm. and had a normal appearance. The suprarenals weighed : the right, 5 grm., and the left, 6·5 grm. The cortex and medulla were well defined. The bladder was unusually large and thick-walled, the prostate rudimentary and the seminal vesicles each about 2·5 cm. in length.

Microscopical Appearances.—The pineal gland was rather cellular, there being less neuroglial fibres and supporting tissue than in the normal adult gland.

The pituitary gland on examination showed an excess of eosinophile and chromophile cells in the anterior lobe. The basophil cells occupied principally the periphery of the gland. Chromophobe cells were relatively few in number. In the pars intermedia, the basophil cells were the seat of a small-celled infiltration. A number of vesicles were present, containing colloid which stained pink with eosin. The pars nervosa (Fig. 3) was nearly as large as the anterior, but showed no structural abnormality.

The thyroid gland had a cubical type of epithelium lining the vesicles and there was a marked degree of colloid storage. There was no fibrosis or evidence

of lymphocytic infiltration. The parathyroid glands were normal in structure. The thymus gland was very vascular and lymphocytes appeared to be increased in number. No Hassall's corpuscles were seen.

Sections of the body of the pancreas showed a slight degree of fatty infiltration lying between normal cell columns. No islets of Langerhans could be identified ; in several sections of the whole block of tissue of more than ½ cm. in thickness not a single islet could be seen. There was no interlobar fibrosis, but an unusual feature was the presence of numerous thick-walled channels completely filled with cells containing dark, oval-shaped nuclei. Tall columnar cells were also present in them lining the vessel walls, which were made up of plain muscle fibres. These channels appeared to be pancreatic ducts, the lining cells of which had proliferated to such a degree as to block completely the lumen.

In the adrenals, the cortex was slightly thicker than normal, but no departure from the normal could be seen in its cell columns. Frozen sections examined by polarized light showed the presence of lipoid substances in the cells of the zona fasciculata. Broster and Vine's stain gave no selective staining.

Both testicles consisted of numerous tubules in none of which was there evidence either of cell differentiation or of spermatogenesis. The cells lining the tubules all possessed relatively large oval or rounded nuclei containing well-marked chromatin granules but no evidence of mitosis. The basement membrane of the tubules were slightly thickened. Between the tubules it was possible to find isolated interstitial cells of Leydig, polygonal in shape, the cytoplasm staining with eosin and their oval nuclei staining darkly by the basophil dye. These interstitial cells were not found in groups, and a comparison with the normal suggested that they were definitely deficient in number. Apart from slight evidence of fibrosis this epididymus was normal. In the prostate many of the tubular alveoli were filled with spindle-shaped cells, apparently derived by proliferation of their lining columnar epithelium.

The liver, kidneys, and spleen were normal in structure ; sections of lung showed changes typical of broncho-pneumonia ; and the heart was in a rather early stage of fatty degeneration.

A more detailed study of the nervous system was carried out. Sections of the frontal grey matter (Economo's area Fe) stained by cresyl violet showed changes which are not unusual in low-grade imbecility—a numerical deficiency of nerve cells with poorly developed processes and irregular alignment ; in addition, there was present a fairly marked degree of subpial gliosis, but the underlying white matter showed no glial proliferation.

In the hypothalamus a study of the various hypothalamic nuclei was made in vertical coronal sections cut in three planes—through the anterior end of the tuber cinereum, through the oral halves of the mammillary bodies, and in a plane immediately posterior to the middle commissure. A comparison of sections with normal control tissue indicated that certain nuclei had suffered a definite reduction of nerve cells and that those cells which had survived in such nuclei exhibited degenerative changes of a chronic character. Furthermore, Holzer preparations showed the presence of a fibrous gliosis involving nearly

the whole region of tuber cinereum and certain adjacent nuclei. Those most affected were the nucleus supra opticus (of Greving), the three divisions of the nucleus tuberis lateralis, the nucleus tubero-mammillaris, the nucleus paraventricularis, and the substantia grisea of the third ventricle. Not all of these cell groups were equally affected. Thus, evidence of cell loss was not marked in the tuberal and paraventricular nuclei. In the nucleus tubero-mammillaris the loss of cells was much less, but pathological changes were pronounced. Even under normal conditions the appearance of these cells is peculiar—large cell bodies with substance aggregated round the periphery and comparatively small nuclei with indistinct nuclear membranes ; but here the morphological appearances were of a most unusual character (Fig. 4), the large nerve cells possessing extremely irregular cell bodies, with ill-defined nuclei, often displaced to the periphery, and in some instances discernible only through the survival of their conspicuous nucleoli. Attached to the margins of the cells were numerous dark-staining processes, some club-shaped and others bead-like or granular in outline, the general appearance being rather as if they were cytoplasmic extrusions. These unusual changes were not present in other nuclei, nor were they found in the small nerve cells of this region, the latter for the most part exhibiting the " severe cell change " of Nissl.

It may be recalled that Roussy and Mosinger (1934) have suggested that in at least four nuclei of the hypothalamus the nerve cells have a secretory function in some ways analogous to that possessed by the chromoffin cells of the adrenal gland, and they claim that it is possible to trace the gradual accumulation of droplets within these cells and their final extrusion into the surrounding nervous tissue. It is possible that the peculiar appearance of the nerve cells described above marked a final stage of a process such as is envisaged by Roussy and Mosinger, but the absence of vacuoles or droplets in these cells and the limitation of the changes to the nucleus tubero-mammillaris militates against the acceptance of such a view, and it would perhaps seem wiser to offer no pronouncement on their pathological significance.

The large nerve cells of the basal optic ganglion exhibited changes in much less degree, some of them having surprisingly little evidence of degeneration. The gliosis likewise showed a remarkable unevenness in extent and intensity. Beneath the ependymal lining of the ventricle there was a moderate degree of gliosis ; in the tuber cinereum the gliosis consisted of a delicate felt-work of glial fibres, nowhere very marked, but on the other hand the basal optic ganglion and the paraventricular nucleus exhibited a gliosis so intense as to be easily discernible with the naked eye in stained sections, the sharply defined dark-staining patches contrasting with the surrounding paler areas (Fig. 5). Under a high magnification, the appearance of these nuclei was very striking, the nerve cells lying in dense baskets of glial fibres (Fig. 6). The glial fibres seemed to have a special relationship to the blood vessels which they encircled, so as to form very condensed interlacements. The vessels, though dilated, showed no structural abnormalities. It was important to note how selective this gliosis was, one nucleus being heavily involved while its neighbour escaped. Thus Meynert's ganglion was free from glial increase, while, as described above, the

supra optic nucleus lying ventro-medial to it was the seat of a gliosis of intense degree.

In addition to the cell degeneration seen in the hypothalamic nucleus, chronic chromatolytic changes were also found in the subthalamic nucleus : several of the cells of this nucleus were binucleated. There was, however, no accompanying gliosis. The nerve cells of the various thalamic nuclei and in the globus pallidus and putamen were much better preserved. Sections stained by the method of Loyez showed a general thinning of myelin sheaths of the nature of a primary degeneration, which was very evident when comparison was made with normal control tissue.

Discussion

It is instructive to trace the sequence of events in this case. A male child, normal at birth except for the presence of a deformity of the external genital organs, developed in his third year an obesity typical of adiposo-genital dystrophy together with a retardation of growth and intelligence. To this picture, at the age of 5 years, there was added a disturbance of water metabolism, the patient exhibiting a very marked degree of polydipsia and polyuria. Later, somnolence appeared, and finally in his thirteenth year a very marked hyperglycæmia and glycosuria were established. In the last year of his life the excessive need for sleep disappeared. The diminutive size of the sella turcica noted radiographically on two occasions, the smallness of the anterior lobe of the pituitary established at autopsy, together with the anomalies of growth and metabolism in this case speak in favour of a diagnosis of pituitary ateleiosis, and it seems likely from the pathological changes encountered in the nervous system that the entire clinical picture was conditioned not by structural alterations limited to the pituitary but by a disturbance of the reciprocal interactions between this gland and the hypothalamic nuclei which regulate its activities. For the view that this disturbance was the outcome of the chronic degenerative changes found in certain of the diencephalic nuclei, there is support in the now extensive literature devoted to the hypothalamus and to the clinical disorders which have been ascribed to lesions confined to its nuclei.

It may be recalled that around the walls of the third ventricle are found a number of nerve cell groups for some of which important vegetative functions have been definitely established ; of these the most important are the substantia grisea centralis, the nucleus supra opticus (of Greving), the nucleus tuberis lateralis, the nucleus tubero-mammillaris, and the nucleus paraventricularis. Furthermore, there is experimental and clinical evidence in support of the view that it is the nuclei of the tuber cinereum—probably the three cell groups of the nucleus tuberis lateralis—which exert a definite influence on the unstriped muscle of the bladder, on the cardiovascular system, on the alimentary canal, on heat regulation, and on carbohydrate, protein, and water metabolism.

On the experimental side, Bailey and Bremer (1921) have shown that, in dogs, puncture of the tuber cinereum can produce polyuria and in some cases adiposo-genital dystrophy. In addition, Houssay (1923) likewise succeeded in producing polyuria by lesions of the tuber in animals with denervated kidneys.

Very similar results were obtained by Camus and Roussy (1920), while Sachs and MacDonald (1925) succeeded in causing polyuria in dogs in some cases by injury to the tuber cinereum and in others by injury to other areas.

Glycosuria, though usually transient and rather difficult to produce experimentally, has been found to follow hypothalamic puncture by Camus, Gournay, and Le Grand (1923), Sachs and MacDonald (1925).

During the past few years the occurrence of polyuria, glycosuria, and adiposo-genital dystrophy following tumours, lesions, and injuries of the hypothalamus has been recorded in papers too numerous to be reviewed here ; the clinical evidence of the important part played by the hypothalamus in the production of disturbances of the vegetative functions of the body seems, indeed, well-nigh incontestible. Unfortunately, in pathological material obtained from the human subject the size or diffuseness of the hypothalamic lesions usually found after death makes the task of determining the exact location of the structures responsible for the symptoms observed during life one of great difficulty, and in the case now reported this difficulty was present ; though three hypothalamic nuclei—the nucleus tuberis lateralis, the nucleus supra opticus, and the nucleus paraventricularis—showed degenerative changes of their ganglion cells, it was quite impossible to determine the order in which they became involved, if indeed they were not all three simultaneously affected. Similarly, with regard to the glial overgrowth, though the paraventricular nucleus and the basal optic ganglion showed a very marked fibrillary gliosis, it was impossible to state whether this morbid process affected first one nucleus and then another, or whether the degeneration commenced at the same period of time in each nucleus.

The significance of the neuroglial proliferation is by no means clear. It has, of course, long been known that nerve cells when attacked by noxious agents undergo a regressive transformation and the neighbouring neuroglial cells a progressive transformation, but it would also appear from recent research that under certain circumstances, at present little understood, a fibrous gliosis of the tissues may be primary. In certain of the hypothalamic nuclei in this case the gliosis was clearly a substitution for destroyed parenchymatous tissue, while in others it appeared to be out of all proportion to the amount of damage sustained by the nerve cells ; that it was the consequence of some form of physico-chemical change can hardly be doubted, though whether the change was the expression of an inherent vulnerability, such as was postulated by Gowers, or whether it was due to some vascular disturbance in this region cannot be determined. The character of the changes in the affected nuclei did, however, suggest a degenerative process of very long standing, and it seems permissible to conclude that the unusual clinical picture presented by this patient was that of an infundibulo-tuberian syndrome.

Summary

A male child, normal at birth save for the presence of external pseudo-hermaphroditism, acquired in his third year a marked degree of obesity which

was followed later by polyuria, polydipsia, excessive somnolence, and finally a very marked degree of hyperglycæmia.

In the nervous system degenerative changes of a chronic character were found in the nerve cells of certain of the hypothalamic nuclei together with a marked degree of fibrillary gliosis.

For the notes relating to the patient's clinical history during the years 1925 and 1929 I am indebted to the Secretary of the French Hospital, W.C.2.

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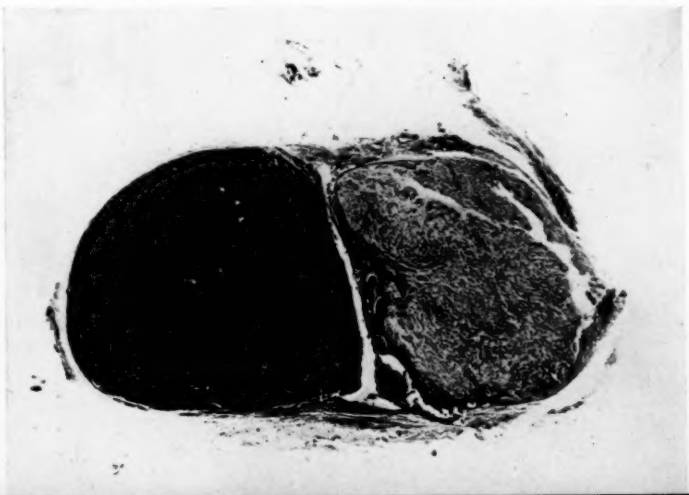
Fig. 1.—Patient, aged 7 years. Note stunted growth and obesity.

Fig. 2.—The patient, aged 16 years, showing obesity largely confined to the thorax and abdomen.



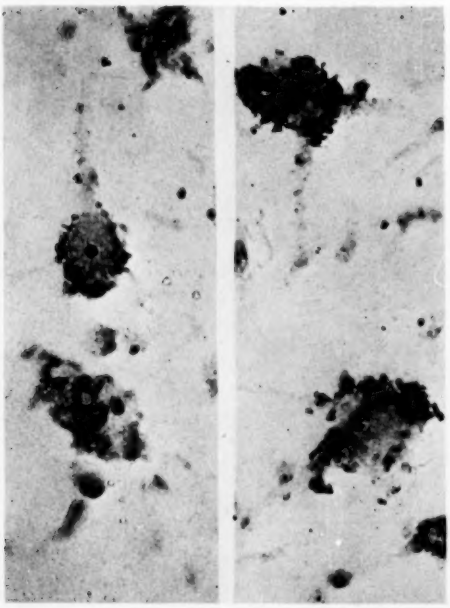


Fig 4.—Nerve cells of the nucleus tubero-mammillaris. Note irregular contour with stumpy processes and lack of definition of the nucleus. Cresyl violet stain ; ×550.

Fig. 5.—Vertical coronal section through the walls of the third ventricle in a plane posterior to the middle commissure. V, 111, third ventricle ; p.n., the two paraventricular nuclei sharply delineated by the fibrous gliosis. Holzer's stain ; ×15.

Fig. 6.—Nucleus supra opticus. The surviving nerve cells are seen lying in a dense entanglement of fibrous glia. Holzer's stain, counterstained with ponceau fuchsin ; ×410.

A CLINICAL STUDY OF STATES OF "ECSTASY" OCCURRING IN AFFECTIVE DISORDERS

BY

E. W. ANDERSON

From the Cassel Hospital, Penshurst, Kent

(RECEIVED 6TH DECEMBER, 1937)

IN this paper four cases are recorded in which certain states of emotional exaltation occurred in the course of the illness. In three of these cases the state in question occurred as an interlude in a depression and in one following a hypomanic state. It is desirable to record these cases, first because of their relative rarity. Janet in 1903 (*Les Obsessions*, p. 380) had only seen half a score or so of such states ; Rümke (1924) found only nine in a series of nearly 5,000 admissions to the Amsterdam clinic, more than half of which were psychiatric cases ; and Paul Mondain (1933) states he had not seen one in four years of mental hospital practice. Secondly, it is desirable to point out the relationship of these cases to affective disorders. This term is used here to avoid the " straight-jacket " of manic-depressive psychosis. The relationship of ecstasies of the type described here, and possibly also many of the recorded cases of religious conversion, to such disorders is not explicit in the literature, although Janet after careful consideration finally rejects it and none of Rümke's cases was diagnosed as manic-depressive. Lastly, while the religious and mystical literature dealing with these conditions is enormous, that from the purely psychiatric angle is relatively scanty. Thus many text-books do not mention them at all and in others the reference is brief. The rarity of these conditions has led psychiatrists to fall back very largely on historical autobiographical descriptions.

First it is desirable to define the word " ecstasy," for the word enjoys no uniform meaning. Bleuler (1924) in his text-book states as follows : " States of rapture are designated as ecstasies. In such states association with the outer world is so completely interrupted that an absolute analgesia exists. The patients see the heavens open, associate with the saints, hear heavenly music, experience wonderful odours and tastes and an indescribable delight of distinct sexual colouring that pervades the entire body." He mentions their occurrence in schizophrenia. Bumke (1929) speaking of ecstasy says that the narrowing of consciousness which one attains in hypnosis shows analogies to ecstasy, that is, to the behaviour of those who are completely preoccupied with one idea of strong emotional tone and who proceed to put this idea into effect without any scruple, forgetting dangers, moral considerations, and the effects of their actions,

but omitting nothing which could further the execution of their purpose (p. 135). Elsewhere he describes ecstatic states amongst epileptics in which they see the heavens open, hear God speaking to them, feel transfigured, or even feel themselves God (p. 642). This may probably be regarded as the classical psychiatric description of the state and is what is generally understood by the term "ecstasy."

Kleist (1928) has described an "Akute expansive Eingebungspsychose" in which an ecstatic state dominates the picture. Fundamentally these are similar states to those described here, but the two cases he quotes belong more to the "classical" psychotic ecstasies already mentioned. One of his patients spoke of having suddenly experienced an "enormous compassion" for the rest of humanity, of an endless love and goodwill, and declared himself willing to offer up his life for mankind. The other had a sudden revelation of the end of the world, felt himself blessed, and also wished to sacrifice his life for mankind. This patient also had visions. The ecstasy was followed by a hypochondriacal depression with anxiety. Kleist regards these cases as very closely related to chronic expansive paranoia with saviour and prophet delusions, and points out that religious preoccupation is commonly found in the premorbid personality and in the heredity. Kleist also believes that such cases are hereditarily closely related to the affective disorders, and also to epilepsy and epileptoid conditions. The states to be described below, however, present features commonly found in descriptions of religious conversion.

Personal Cases

CASE 1. Miss ——, æt. 23 (Jewish).

Family History.—The elder of two children, brother aged 21. The mother suffered from fits of moodiness in earlier life, but is now more stable. A maternal aunt was described as "highly strung." A maternal uncle was odd, hypochrondriacal, and a crank. The father's sister had a breakdown, nature unknown, 20 years previously. The father was stable.

Personal History.—She was a healthy child, but was late in learning to walk. She had whooping cough, measles, and tonsillitis in childhood, otherwise no serious illness. She was a difficult child, bit her nails, and had nightmares. At school she was backward, had difficulty in learning to read and write. She was at several schools where she did not get on with the other girls and was removed by her mother. She disliked school intensely. Quite early she showed an aptitude for music and on leaving school commenced its serious study, but could never work consistently and failed to take her diploma. After six months' residence in France she could hardly speak a word of French. She was timid and shy. She conceived violent attachments to people and there was a history of a homosexual friendship, whose influence was still significant at the time of admission. For about two years before admission to hospital she had been on bad terms with her mother, to whom she was abusive. On account of her abnormal behaviour she was seen by a psychiatrist, who advised her removal from home. She stayed with a family, but there was friction and she could not get on with anybody. Finally she was referred to the Cassel Hospital.

Mental State on Admission.—She was elated and over-active, meddled in other people's affairs, and proved a nuisance. She was, however, good-natured, affectionate, and could be managed with firmness. There was no evidence of anything grossly psychotic, but there was a distinct paranoid component in the sense of mild ideas of reference—thought others were criticizing her, which was possibly true, and which in her

case had in part a pathological basis in her sensitiveness. There were some obsessional features, such as extreme tidiness and exaggerated conscientiousness. She was troubled by silly phrases running through her mind, e.g. " to cater for a King." Her moods as described by her showed a definite alternation between depression and elation.

Soon after admission she became more calm, during which phase she had the experience described below. She said that she had had a kind of religious conversion. One day when working in the garden she suddenly felt " very uplifted "—an " ecstasy." She felt the world increased in beauty, everything was more real—" the beauty of reality. There wasn't any phantasy about it, the realization of all those things being more beautiful than I could conceive myself." She felt her ability for the task in hand was of the nature of an inspiration. At this time she saw two trees growing together, and this taught her a lesson that " one need be neither a martyr nor an aggressor." Since the ecstatic experience she had felt calmer. She spoke with God the whole time, " not an actual voice, but a knowledge of just exactly what to do." The ecstasy described lasted about six weeks with fluctuating intensity.

The state may now be described in greater detail. She said : " I just didn't mind anything ; nothing mattered which anybody did to me, it didn't disturb me. I just felt at the time it was a right state to be in and that everybody ought to be in that state. I thought I was even going to become weller than even people who thought there was nothing the matter with them any way." In this state she felt she could convert an apparent disadvantage into an advantage. " The thing is that when I'm feeling miserable I think to myself, ' Is the whole thing a dream ? ' I can't come to a true realization of my troubles. I'm absolutely certain it's wrong when people say it's too good to be true, for the happier I am the more I'm conscious it's real." (You said things seemed more in detail ?) " Well, they did seem in more detail because I was noticing more. One day I went into the wood and saw the individual grasses standing up ; there was no stagey scenery about it. Nothing that anybody could make would be like those grasses. There's so much picture-making in the world that people are inclined to look at a thing and say it's picturesque and see it on the flat side, instead of looking at it and saying it's very natural and very real. If people saw things actually as real as I saw them they wouldn't want a picture."

Alteration of time perception was present : " I just lived in the present without worrying about the past or . . . the future. You absolutely have to be living in the present to get that feeling. I didn't care how long I was kept waiting for anything. I gave up thinking in time at all. I didn't watch the clock any more. It gave me more a sense of being than of doing." The feeling of being merged in the cosmos appeared in experiences like these : " You just have the feeling you're part of the earth, not a person on your own, sort of melt into it." (The whole earth ?) " It's a kind of sympathy and fellow feeling for all the things, trees and birds and everything, and a feeling of harmony, just part of it, there's nothing you could want more than that, certainly not at any time."

During the ecstasy her compulsive feelings disappeared or were modified. For instance, she still had a compulsion to do things " for her conscience' sake," but enjoyed doing them. She also enjoyed doing things for other people and felt friendlier towards everybody. It is to be noted that the ecstasy left behind it an alteration of the personality, a feeling that things were more real than they used to be ; but this disappeared when she was very depressed.

The state of ecstasy was replaced one evening by another which she described as follows : " I thought things had gone dead and the birds flying in the sky seemed dead, I thought things were worse than before, but I think it was just the ordinary way." She felt the " flickering back of time, sort of went back like this " and here made a sudden gesture.

Progress.—Her mental state reverted to that observed on admission and she showed, as before, fluctuations in mood. There was no recurrence of the ecstasy.

A few months later she was discharged, but there was no fundamental improvement to record.

CASE 2. Miss ——, æt. 30.

Family History.—The father, a clergyman aged 65 years, was described as of "nervous temperament" and tending to worry over trifles. He suffers from diabetes mellitus. The mother, aged 64, had a depression of religious colouring with self-reproach some years previously. The patient is the second of three—the other two are brothers, the younger of whom suffers from tuberculosis and at times becomes depressed and at others extravagant. One child by a former marriage of the mother appears to be healthy.

Personal History.—An eight-months child, she was delicate and did not talk properly until 5 years of age. At this time she wept if anybody spoke to her. She suffered from enuresis till 8 years of age, and had the usual exanthemata. Appendicectomy was performed at 12 years of age, and later the tonsils and adenoids were removed. Her periods were regular, but had been painful during the year before admission. The patient attended a High School and left at 16 years of age. She was evidently not scholastically brilliant, but good at games. About this time she had an attack of depression with depersonalization which shortly cleared up. She then took up ballroom dancing as a career and taught it for a few years, but gave it up because of ill-health, which from then on interfered almost continuously with her activities. At the age of 21 she developed symptoms of hyperthyroidism which yielded to treatment. Her first ecstatic experience occurred at this age following the "laying on of hands." She felt uplifted and experienced "perfect content, perfect peace." At 23 years of age she developed attacks of tetany, in association with hyperventilation of a psychogenic character. The present illness began three years ago, when she became "yellow and thin," had abdominal distension, nausea, anorexia and palpitation, and felt very weak. She became depressed and depersonalized—"people seemed to be shadows, I didn't know where my voice was coming from, it didn't sound mine." After a few weeks' treatment in a nursing home she felt little improved. Soon after this the patient underwent a conversion experience while attending a High Church Mission. A few days later she made her first confession, after which she felt blessed. This was the beginning of a state she described as follows: "I just felt very peaceful and happy, very contented; and I felt that every little thing I did, things that were ordinarily irksome, were a joy to do; and because I loved God I felt He was in me and I felt I wanted to go out and tell the world about it. I didn't actually see a Cross, but I was always conscious of the Cross and from it came the most amazing love and power." The experience dominated her consciousness. She felt as if she had been born anew, and saw only good in others. Everything had increased beauty, and "everything seemed to speak of God. The Presence was real."

The above state came on abruptly, gradually increased in intensity, and remained so for about a year. During the period of ecstasy she had a love-affair with a married man. There was a certain amount of intimacy, though sexual intercourse was denied. She became depressed and developed much conflict and self-reproach over this affair, as it was contrary to her principles. The depression became intense, and at the same time the state of ecstasy disappeared. Gradually the depression cleared up. One year before admission she had a febrile illness diagnosed as influenza, with severe occipital headache, followed by a septic throat. After a slow recovery she took up social work. She felt, however, that she had returned to work too soon and began to feel "confused, and unable to concentrate." Depression and irritability set in and her gastric symptoms again became prominent. She again became "very thin and yellow" and had some depersonalization. There was a moderate pyrexia. On swallowing bismuth for an X-ray examination she had a psychogenic attack in which she went "cold and shivery" and lost the use of her legs and hands. An exhaustive physical examination proved negative.

Mental State on Admission.—She seemed mildly depressed and a little listless. Beyond this, however, there was nothing grossly psychotic. She had neither delusions nor hallucinations. Her memory showed no impairment. She mixed well in the social life of the Hospital and presented nothing obviously striking in her behaviour.

It was evident at this time that she had already improved and a few weeks later she was discharged from hospital.

CASE 3. Miss ——, æt. 27.

Family History.—The father, aged 83, was described as " nervous " and over-anxious. The mother, aged 68, was pessimistic, prone to worry, afraid of going out, and suffered from nervous dyspepsia. The patient was the last of a family of six, besides one half-sister by the father's first marriage. The eldest of the six had a depression of religious colouring from which she recovered, but remained over-anxious about her health and has still conflict and doubt in religious matters. The third sister at 15 years of age had impulses to do certain things and compulsive and blasphemous thoughts for a year. She now shows an exaggerated conscientiousness. The fourth, a brother, was unstable and drank heavily for a time, but has settled down satisfactorily. The fifth, a sister, has attacks of depression without obvious cause and is usually apathetic. A maternal aunt had " religious mania " and is subject to " fits of laughing and crying."

Personal History.—The patient was a healthy child, but had pneumonia when 3 months and rickets when 1 year old. About 15 years of age she developed a slight spinal curvature. She had influenza badly once or twice. Formerly she had headaches with nausea lasting a day. Catamenia commenced at 13 or 14 years, and were regular, but profuse and somewhat painful. At the periods she was either more depressed and irritable or more energetic. The patient attended a public school for two years, where she felt that she could never cope with anything, and was taken away by her mother because she was unhappy. She was then taught by a governess. Never trained to any employment, she has lived at home since leaving school. Her sister described her as unstable in mood, by turns happy and depressed, as being affected, and always acting a part. She showed a superficial versatility in music and writing and had mystical and religious interests. She had few friends and was very self-centred. She had several minor love affairs ; one important attachment of a pathological nature will be described in detail below. Masturbation and spontaneous orgasm on reading or seeing anything of sexual content had occurred on frequent occasions. The patient had always felt depressed and inadequate. About puberty her depression became more noticeable, and obsessional symptoms which had been present since early childhood became intensified ; for instance, when putting away any article she had used she was compelled to think of it in all its aspects and relationships and she also had a " délire de toucher." At 15 years of age she fell in love with a married man of lower social class. She knew this man by sight for three years before making his acquaintance, after which there was a good deal of intimacy, though sexual intercourse was denied. The man's wife found out this intimacy and protested to the patient's parents, who held very strict views. This proved the starting-point of her worst symptoms. After the rupture she was said to have " gone to pieces," slept badly, had fits of violence, and showed some hysterical behaviour, such as claiming falsely to have vomited blood. When the affair was broken off the patient stated that she passed into a state " like delirium." She recognized her surroundings, but could not describe them. She said " her whole personality seemed in disruption." This state gained in intensity, and at its height she acquired an abnormal power of detachment, though noticing every detail of her environment. " I seemed to be . . . watching myself." She also spoke of " a feeling of lightness and buoyancy, as if anything might happen." This lasted two days and was followed by a state of ecstasy of which she had three before admission. The first lasted from

10th November to the end of December, 1931, the second the whole of February of the succeeding year, and again in the autumn of the same year for three months.

These states all presented similar features. She described the experience as follows : " I seem to merge into everything." There was " an intense consciousness of power and absolute ecstasy. I am awake all night if I happen to have it, sometimes it wakes me up. It comes in a sort of flood . . . over the body. A terrific consciousness of power in surges, like the sea coming against you." She also felt an excitement and palpitation, but added, " I feel calm as well. Things appear more real, as if you were just becoming alive and had never lived before. The whole being expands. If you are alone and you yield to it the more it grows over you, and you feel you can't keep on the ground. Everything is much more intense ; I notice everything I haven't seen before, lights and sounds." She felt as if she were in touch with God and felt she could " get at the back of everything." " You want to give yourself up to it because it seems as if something finally happened you would lose yourself, but it seems as if will seems to get in the way." She noticed a change in her perception of time. She had no sense of time, " everything is absolutely new, every minute is as if everything has just started." Time seemed to go quicker and she felt she had " all the time in the world to do things in." " I seem above time and yet it was intensified in some way. I could see time for what it was. It seemed like something which served a purpose, which was used to divide, to limit something, but not real." Yet her sense of everyday time was the same. " I seemed as much in the past and future as I was in the present, not only my own past and present but everything " (i.e. the whole of history). " It was the same with space, and to think of any place was almost as if I were there, I seemed so identified with it." In these states anything she wanted to know seemed answered, everything seemed natural, and she could see everything in its correct relationships. She felt also she had a sense of humour.

Her attitude towards her lover changed. She felt she could give up everything, that nothing had a hold on her any longer.

These states came without any warning and only when she felt " utterly to pieces," and she added that when she began to feel better in an ordinary way they disappeared like a tide going back. No heightening of sexual feeling was noted in the ecstasy. During the ecstasy her compulsive thinking disappeared and also her menstrual troubles. The condition " like a delirium " which preceded these ecstasies always followed them. Since the last ecstasy she had become progressively more depressed and complained of things " closing in on her." This state became intensified at times and after one such attack she had a phase of increased energy, which passed after a week or two. A few months before admission she became very weak and was finally admitted to Hospital.

Mental State on Admission.—She looked desperately serious, felt exhausted and rather sick, but denied feeling depressed. She complained of the obsessional symptoms mentioned. There was no evidence of delusions or hallucinations, though on two occasions some years previously she had heard a voice, once calling her name. She felt as if she were " possessed, bodily and mentally." Orientation and memory showed no impairment. She had a moderate grasp of general information and was tolerably intelligent. She had threatened suicide on several occasions, but had made no attempt.

Progress.—Her condition remained more or less stationary, but she showed fluctuations in mood and was sometimes very depressed. At times she felt she was losing her personality and became identified with people she met. She had to be by herself for a time before she felt she recovered her own identity. At times also she felt herself merging into objects, for example, she felt she was becoming one with the chair on which she sat. She felt " fluid " and that the substance of inanimate things was alive. At times also she felt her hands became larger. She felt " miles away " from her surroundings and objects appeared very small " like doll's house things." Sometimes she felt she was growing smaller and " dwindling."

On 4th July, 1937, she had another ecstasy which she described as follows : " A stillness gradually came over my whole being and a sense of expectancy impossible to put into words. . . . There seemed a trembling vibration over my consciousness, a veil between me and what I should know, as if I were hovering beyond a great mystery. Then a dawning sense of exquisite harmony, without being lifted into the first state of ecstasy. . . . Thought, space, and time dropped away. . . . "

This experience occurred at 11.30 p.m., came suddenly like its predecessors, and lasted for about half an hour. She did not report it until the next morning. She was then calmer and felt " more normal." On the morning of the 5th she said : " I feel as if my thoughts and worries are gone." She perceived a sense of " harmony and rhythm " not only in herself but in everything else like " a flowing " : " it seems as if everything's flowing and I'm in it." She also felt a little abstracted, which she had not felt in the more intense form of the experience. This ecstasy differed in some respects from its predecessors : " a sense of it without being in it." She felt " partly depressed," which she believed was because the ecstasy was not as intense and complete as its predecessors. She had, however, even in this brief experience felt herself at one with the universe, but not to such a degree as before, and it was experienced less as " merging " than as a sense of harmony. In this state she also had a feeling of strength which persisted to the following day. In her own words " the other ecstasy was an overwhelming sense of happiness, this time I feel more calm and have not the same sense of activity." When seen the day after there was outwardly no change in her, certainly no objective increase of activity. She described a change in her thinking. Before the ecstasy she had " a rapid flow of thought." When the ecstasy supervened it seemed " as if the thoughts flowed away " and left her with a sense of stillness. The rhythm of her thinking and the rhythm of the whole environment coincided. The next morning she still had the sense of immensity which she experienced in all her ecstasies. The patient has always been preoccupied with the question of what a normal state is like. She thought that in the normal individual this harmony between him and his surroundings existed without his being conscious of it, and it was just this consciousness which differentiated the ecstasy from the normal.

On the 7th the patient again felt depressed and " panicky " and was " oppressed by a sense of guilt," but again the same evening she stated as follows : " I had a sense of that state without being in it. I felt happier—in harmony—at rest without being overwhelmingly conscious of it ; feeling as if the mind and body are more harmonized. " The recent occurrence of an ecstasy seemed to have enabled her to analyse her experience better. The difference in the " merging " in the ecstasy is that in this state it seems as though everything were coming into her, associated with a feeling of forward motion, " something calming and then a sense of everything moving into me." In her depressed state " as if I'm being dragged back and dissolving mentally and physically and outside all motion." The patient vouchsafed the information that in the ecstasy everything inanimate seems to be moving and added " motion seems to give the object its form. Before this everything seemed separate, there was nothing binding it together." In the depressed phase " motion seemed to be lessening and hadn't any existence. I could see the things, but I was outside the consciousness of any sort of life at all, an abyss. . . . It seemed as if there never was and never could be any sort of motion at all."

Since this ecstasy her mental state has reverted to what it was before.

CASE 4. Mrs. ——, æt. 39 years.

Family History.—The father, who died, aged 53, from phthisis, was described as very conscientious. The mother is alive, aged 58, happy-go-lucky, cheerful, and rather dependent. The patient is the eldest of four, the other three being normal. The paternal grandfather drank heavily. Beyond this the family history was essentially negative.

Personal History.—The patient was a healthy child and developed normally. There

was no history of neuropathic traits. Beyond childish ailments she had no serious illness until 16 years of age, when she had a brief attack of depression. At this time she became interested in religion, which interest has continued, though less strong. She had a high-school education until aged 17 years. Her school record was good ; she played games well and had no difficulties. On leaving school she taught for a time and then took up nursing, which she had to give up because of " adhesions " following appendicectomy and removal of an ovarian cyst at 18. For a few days previous to her periods, which were regular, she was depressed.

She was ordinarily cheerful and sociable, though she worried and took the troubles of others to heart. Her mood fluctuated. She had many interests and read widely. At 23 years of age she married a man some years older and had two children and between them a still-birth. The marriage was not particularly happy. She had a pelvic repair operation a year after her first confinement and later an amputation of the cervix. Her last delivery was by Cæsarean section. Four years before admission she had an attack of pleurisy, from which she slowly recovered. She became depressed and developed a sobbing breathing. She remained depressed for two years or so, during which she was treated by psychotherapy. Improvement took place until the onset of the present illness at Christmas 1934. She began to feel run-down and developed influenza complicated by an otitis media, three months later phlebitis with low fever set in. Serious chronic illness was suspected, but excluded. She complained of lack of energy, became depressed, and felt she " wanted to get out of it." For this disturbance she was admitted to the Cassel Hospital.

Mental State on Admission.—She was slightly depressed, was self-reproachful over a recent sexual episode, and complained of a " mental tiredness." There were no delusions nor hallucinations. Orientation and memory were unimpaired. Her intelligence was above average. At times the difficulty in breathing reappeared, always in relation to an unpleasant event.

After four months in Hospital, during which her condition slowly improved, she passed abruptly into a state which she described as follows : " The first and most persistent impression was one of great tranquillity and freedom from anxiety and an underlying conviction that this condition was unassailable. I was very remote from my natural surroundings and the entrance of people was a nuisance, as I had to pull myself away from the realms of bliss and make some effort to cope with facts which seemed unreal. People did not disturb the state except in so far as it meant coming out of it temporarily. They seemed vaguely unreal and it was I who was real. An international event of some importance which occurred while I was in that state floated into my mind now and then in such a way as to make me think I had dreamt it. Gradually there crept into the sensation of tranquillity a vivid impression of sunshine and summer at its best. I wandered or rather floated in flowered meadows and gardens. The thought now and then was, ' This must be where the idea of the Elysian Fields originated.' All the sensations of a perfect summer's day were present, the hum of the bees and the clear brilliance of the atmosphere. As I dislike the really hot weather it was evidently early summer, as the feeling was of perfection. The flowers were many and perfect—almost artificial in their perfection, and the fruit also. The colours were violent, almost crude, and it was almost as if everything had had a coat of varnish. I was quite alone in these wanderings and there was never an impression of anyone else being present. Time passed quickly and I was unconscious of its passage. Periodically, say at meal-times, I looked out of the window to assure myself that the trees were leafless, and metaphorically ' pinched myself ' to see if I were awake. This condition lasted for six days, diminishing towards the end." During this experience she was outwardly calm and unperturbed. A few weeks later she was discharged improved.

Discussion

Views on the Nature of States of Ecstasy

The states described by the first three patients correspond to the phenomenon designated by R. M. Bucke as " cosmic consciousness." Bucke had himself undergone an experience which he described as follows : " The prime characteristic of cosmic consciousness is a consciousness of the cosmos, that is, of the life and order of the Universe. Along with the consciousness of the cosmos there occurs an intellectual enlightenment which alone would place the individual on a new plane of existence—would make him almost a member of a new species. To this is added a state of moral exaltation, an indescribable feeling of elevation, elation, and joyousness and a quickening of the moral sense, which is fully as striking and more important than is the enhanced intellectual power. With these come what may be called a sense of immortality, a consciousness of eternal life, not a conviction that he shall have this, but the consciousness that he has it already."

Elsewhere he says : " I was in a state of quiet almost passive enjoyment, not actually thinking but letting ideas, images, and emotions flow of themselves, as it were, through my mind. All at once . . . I found myself wrapped in a flame-coloured cloud. . . . Directly afterwards there came upon me a sense of exaltation, of immense joyousness accompanied or immediately followed by an intellectual illumination impossible to describe." (Quoted by James, 1908, p. 398–9.)

This state only lasted a few seconds. Edward Carpenter, who had a similar experience, regarded it as a third and highest state of consciousness, differentiated from the simple consciousness of very young children and primitive men and the self-consciousness or consciousness as we ordinarily understand it in normal adults. In the stage of " cosmic consciousness," he says, " the object suddenly is seen, is *felt* to be one with the self. . . . This form of consciousness is the only true knowledge—it is the only true existence . . . in which the subject and the object are felt to be parts of the same being, of the same including self of all."

Experiences of a like character have been recorded by mystics of every religion. Crichton-Browne (1895) described under the title of " dreamy mental states " a group of depersonalization phenomena which he related chiefly to epilepsy. He also mentioned the states with which we are concerned and quoted a passage from J. A. Symonds, who described his experience. Crichton-Browne says this writer was " haunted by melancholy " throughout his life. James (1908, p. 380) set up four criteria of the mystical ecstatic state, namely " ineffability," " noetic quality," " transiency," and " passivity." He regarded the first two as the most important and constant. By " noetic quality " he meant that perception of increased and hitherto unguessed meaning in things, for he stated " they are states of insight into depths of truth unplumbed by the discursive intellect. They are illuminations, revelations, full of significance and importance. . . . " He believed that mystical states were not long sustained and regarded an hour or two as the limit. With regard to the last quality

James (1908) stated that the mystic " feels as if his own will were in abeyance and indeed sometimes as if he were grasped and held by a superior power." Mayer-Gross (1914) differentiated two types of emotional experience, which he designated " Glücksrausch " and " Glücksaffekt." He set up differential criteria, one of which was that in the former the subject was given over entirely to the emotion to the displacement of other objects of consciousness associated with a more or less complete passivity, whereas in the latter there was an intensification of the ego associated with an urge to action and a feeling of increased capacity. Whether these two states can always be so clearly differentiated is doubtful, and the cases given here present features of both. Janet (1926–28) observed a patient over a number of years in the course of whose illness ecstatic interludes occurred. The ecstasies of this patient corresponded closely with the classical descriptions of the state. Janet distinguished three degrees in the ecstasy, which he designated " recueillements, extases, and ravissements " (p. 45). He noted the complete suppression of motor activity in his patient, the feeling of a " sort of possession," the sense of certitude, of internal peace and power, and the feeling of ability to solve all problems and answer all questions. His patient also described the great " luminosity " of her visions. He gives as the essential criteria of the ecstasy state the complete immobility and detachment from outside things, the enormous internal activity, the intense faith in the reality of what is experienced, the profound feeling of automatism and inspiration, and the special feeling of joy (p. 137). Janet also regarded what he called the " sentiment du divin " (p. 127) as essential and stated : " The true ecstasies are the religious ecstasies."

Gruhle (1922) stated that there were only two conditions, true epilepsy and schizophrenia, in which such states of ecstasy supervene without the assistance of inner or outer agents. He stressed the qualitatively abnormal feeling in ecstasy and said that the feeling of joy was more than a heightening of the normal feeling of happiness and that the essential feature was the peculiar linking of feeling with knowledge. He mentioned the frequent occurrence of such states as a precursor of an epileptic fit. Further, he wrote that the states of bliss which occur in schizophrenia could not be qualitatively differentiated from those in epilepsy, and mentioned the visual hallucinations and heavenly manifestations occurring in each. He gave examples of the different forms of ecstasy, including those following the so-called spiritual exercises of the Buddhists and the ecstasies produced by intoxicants such as mescal and opium. Jaspers (1923) recognized the wide range of degrees of intensity, from purely sensuous feelings of joy to the religious mystical states. He mentioned that " sublime feelings " occur phasically in psychasthenics, but the more intense ecstatic states characterized by a feeling of grace and blessedness together with the perception of heightened significance in things in schizophrenics. Flournoy (1915) described a woman who experienced typical ecstatic states. This patient showed a marked dissociative tendency, as shown by automatic writing, clairvoyance, etc., evidence of that peculiarity of the ego (Ichlähmung) which is responsible for similar phenomena such as glossolalia and possession and is an important factor in the psychopathology of the states under discussion.

Rümke (1924) found clinical features similar to those in the present material in his cases. He devotes little consideration to the time-disorder, which is not prominent in his material. He finds the difference between these states and those of mania to consist in the alertness and greater superficiality of the manic, whose disorder he relates to a less profound disturbance of the ego. He regards a state of inner tranquillity as *one* essential factor in the causation of these conditions. He found that these states occur principally in complicated psychoses, which is in agreement with my own observations. His cases, however, were all much more severe than mine. He regarded the syndrome as prognostically favourable, apart from the clinical diagnosis of the case as a whole, a remarkable statement which finds no support from the present study. In agreement with Janet he found religious feeling an essential part of the state. He was unable to find a causal explanation of the condition in the preceding state, and noted a contrast between the state of bliss and its precursor. He found that a motivating factor played a very small part in the genesis of these states. He found that this syndrome occurred seldom or never in manic-depressive psychosis. Rümke bases his study on the psychology of Scheler and finds a confirmation of the latter's views. Rümke regards the conditions discussed here as belonging to the category of the " Geistige Gefühle " which involve the very core of the personality.

Psychoanalytic writings on ecstasy are few. Glover, in a hitherto unpublished paper on " Idealization," speaks of the tendency in some patients to excessive idealization of their natural surroundings. It is not clear, however, whether his " idealization " corresponds entirely to the states described here, and he gives no description of similar prolonged states of ecstasy. Alexander (1931) described the Buddhist path of initiation and saw in it a reversal of the normal psychic development as conceived by the psychoanalytical school. He claimed to recognize in it the catatonic ecstasy of schizophrenia. Thouless (1923), speaking of " mystical conversion," states : " It is not only that part of the libido specialized in the sex-instinct that is sublimated, but the whole of the libido employed in the activities and affections of this world life." Geiger (1911), in an analysis of æsthetic appreciation, has shown that in one form the " Einfühlende Einstellung," a union of the ego with the object, occurs. He showed that the process involved an activity on the part of the observer's ego which is lacking in the conditions described here, where the ecstasy appeared without any conscious striving. It is evident, however, that the same essential psychological phenomenon occurs in both cases, and it may be that some few individuals actually experience a type of ecstasy in the contemplation of artistic works, more particularly of music. Lastly, Zucker (1934) regards the Shamanistic experience as a " participation " experience, as Lévy-Bruhl terms it (p. 344), that is, a state of consciousness in which the sense of duality of subject and object is abolished. The subject is at the same time aware of his own identity yet feels himself identified with the object. Zucker continues : " In this experienced unification of subject and object, in this 'veritable possession' where the psychic state of interrogation and the will to answer coincide, lies the possibility of a liberation and a satisfaction of both." Zucker says the answer is experienced

intuitively (*erlebt*), not logically deduced. It is clear that we are dealing here with a psychic state closely corresponding to if not identical with ecstasy.

A review of the literature demonstrates thus : the comparative rarity of these states, the existence of different types of " ecstasy," and the frequent statement that they are common in schizophrenia, epilepsy, and hysteria. Their occurrence as a phase of manic-depressive illness is not mentioned. Psychopathologically these states are characterized by a peculiar feeling of joy (Glücksgefühl) consisting of a remarkable blend of feeling with knowledge. The amount of psychiatric attention, however, which they have so far received is slight, and it is clear that the whole field requires more study, particularly perhaps the relationship between these states and other emotional states occurring in the realm of the normal.

Features of Personal Cases

A calmness and tranquillity was reported by all the patients, and in the first case was associated with a definite decline in motor activity noticeable after the previous hypomanic state. None of the cases showed the complete immobility of Janet's patient. Passivity, associated with a feeling of " merging " into external reality, was most noticeable in the first and third patients, whilst the second spoke of God as " being within her." The fourth subject differed in that the external reality seemed less real, as in depersonalization, whilst the ego was experienced with a heightened reality. Also there was no merging with external reality, although the feeling of passivity was present. This sense of the self as the only reality was also experienced by Symonds, who wrote : " At last nothing remained but pure absolute abstract self. The universe became without form and void of content. But self persisted formidable in its vivid keenness . . . " (quoted James, 1908). This experience is not quite the same as that of the fourth patient, who had no sense of impending dissolution of identity.

The feeling of being amidst unseasonably beautiful surroundings, constituting a kind of extension of the " ego " and separating the patient from the outer world, which she always felt was intrusive, was not hallucinosis. Janet's patient also saw the outside world transformed at times in a similar way. In cases 3 and 4 the passivity was clearly experienced in terms of volition. The state of passivity receded in the third patient whenever her will asserted itself, and in the fourth patient diminished in intensity whenever she had to bring herself back to earth.

The feeling of merging with the environment described by some of the patients is, however, not peculiar to ecstasy alone. The third patient experienced it while in a depressed state, but in a different way. In the ecstasy the feeling of " merging " gave her a sense of gain : " as if I found myself and everything else." In the depressed state she lost herself : " I feel my thoughts go and as if I shouldn't be able to move, as if I were sinking into something." In the ecstasy she had a greater sense of identity, the lack of which feeling was usually a constant and prominent complaint. For her the ecstasy consisted of

a sense of union with separateness. She further spontaneously divided the ecstasy into three stages, first a feeling of immensity, secondly a feeling of " terrific activity " behind each object, as if everything seemed moving and she were moving with it, which was finally followed by a feeling of " being centred on something." During this phase her thoughts were " terrifically active," a " sort of terrific calm and yet active." She was conscious, however, of no pressure of thought. It is interesting to note that in contrast to the relative decrease of motor activity of the first patient during the ecstasy, this patient became more active, although after the last ecstasy her sense of activity was diminished.

The change in the external world was a noticeable feature in all four subjects. The first three patients observed that everything seemed more beautiful as well as more real, and more intense, that details were perceived which had not been noticed before. The first patient saw " the individual grasses standing up." With regard to the " sentiment du divin," the first and the third patients, in contrast to the second and fourth, were not strongly religious before the ecstasy. Both, however, experienced the nearness of or rather the identification with God. It appears therefore that a strongly religious bias is not essential even to the content of the ecstasy. One must, however, agree in general with Janet when he says : " Les idées et les sentiments religieuses font partie de la définition de l'extase complète," with this qualification, that if by this is meant that the subjects become aware of the nearness of, or more properly identify themselves with an immense cosmic power at first outside themselves, then this may be accepted as an essential feature, though undoubtedly there are some types of ecstasy or ecstasy-like states, as that of the fourth patient, where this feeling, despite a definite previous religious attitude, did not occur. The fourth case, however, is atypical. It is to be expected that the religious beliefs of the subject will exert an influence on the content of the ecstasy.

The experiences of these patients are paralleled by others of which many historical biographical instances have been recorded, the details being remarkably constant from case to case. In abstracting common features, some variance with other authors arises. To take James's criteria, the lack of descriptive ability is certainly a common feature. It also occurs in a large number of pathological mental states and only appears striking here because of the strong urge to communicate these emotions. The passivity of the subject is one of the most striking and essential features. Such ecstatic states may last for a long time, up to a year. The " noetic quality " emerges clearly. Janet stresses immobility as an essential feature, but this was not characteristic of the cases recorded here.

Disorder of Perception of Time and Environment

One constant feature in these cases is the alteration in perception of time. The third patient was conscious of the purely arbitrary and practical value of mathematical time which she also felt went more quickly. She stated : " I didn't feel limited by it (time). I felt it was something I was using, not some-

thing which existed." The feeling of being one with the cosmos is well expressed by the statement of the third patient, that she seemed as much in the past and the future as she was in the present, not only her own past and future, but the past and future of everything. She felt that past and future telescoped to a point, the present. The first patient said, " I just lived in the present without worrying about the past or . . . future " ; the second patient felt " born anew " ; the third felt " as if everything had just started," as " if she had never lived before " ; and the fourth patient felt that time passed quickly. This is in contrast to the experience of time in some cases of depersonalization, in which time becomes a dreary eternity for the patient. In depersonalization the past is perceived at times as almost endless, whilst the future seems remote, which Janet regards as typical of this state. The feeling of being reborn occurs repeatedly in other descriptions of these states, and is regarded as the central point of the conversion experience. It is also, of course, common in schizophrenia. Janet and Flouroy also noticed the change in time perception in their patients. Janet's patient no longer distinguished the past from the present, and Flouroy's patient felt that she had plunged into eternity.

In ecstasy these subjects live entirely in the glorious present, which, as it represents perfection, requires no count to be taken of the past with its failures nor the future with its hopes and expectations. They have attained that beyond which there is nothing better. Or it may be said that the present is so real and claims their attention so exclusively that past and future have no significance. Janet considers that this transformation of time is brought about by the indifference to external action, as in his patient, but this explanation does not hold in the case of the third patient, who, as we have seen, became more active externally. Of the sense of duration he says elsewhere that the " sentiment d'effort spécial " engenders all our ideas of time (1926–28, II, p. 611). In ecstasy, where everything seems effortless or nearly so, time is experienced as passing quickly.

Similarly the change in the environment both in these patients and in other recorded instances is constantly expressed. Also they speak of the greater beauty of everything and the greater feeling of friendliness and sympathy for others, which was most striking in the first patient, in whom the paranoid attitude completely disappeared.

The feeling of buoyancy and lightness experienced by the first patient is also mentioned in an example by R. W. Trine, who says of his subject : " this spirit of infinite peace so takes hold of and so fills him, that it seems as if his feet could hardly keep to the pavement, so buoyant and exhilarated does he become by reason of this inflowing tide " (quoted James, 1908). This subject and the third patient both speak of the experience as of a " tide." Janet's patient had similar experiences.

The memory which the subject retains of the experience and its subsequent effect on the personality must be considered. Practically all authors are agreed as to the vivid memory retained of these states. This is equally noticeable in the cases presented, as some of the descriptions were given after the experience. It would be remarkable if such an experience did not make an indelible im-

pression. It would appear that the personality of the third patient is little modified by the experience. To her it simply remains a remarkable and abnormal experience. Though stress is laid in the religious writings on the spiritual value of such an experience, it has not meant anything of the kind to this patient, nor has it modified her conduct. For a change in conduct to result the subject must be strongly religious or else have a desire for faith. This religious preoccupation need not be entirely conscious, as James points out (1908, p. 230 ff.), but if it is present at all, the ecstasy experience results in a fusion of conflicting elements in the personality, which remains more or less permanently modified by it. The intensity of the ecstasy experience in itself would not appear to be sufficient to induce this modification of the personality. This feeling of merging with a greater power outside the subject, however, is usually interpreted as union with " God " or universal spirit.

It seems probable that the impression on the first patient was more profound and remained with her as a glimpse of perfection, except when she became extremely depressed. It is doubtful if the experience had any essential influence on her conduct. In the second case the ecstasy became a true conversion experience of which the religious background was a vital factor. It is interesting to note the different valuation which the second patient gave to the two states, the ecstasy and the subsequent depression. The former was a spiritual experience, a revelation of the Holy Spirit, and was regarded as healthy if unusual ; the latter as illness and a just reward for her backsliding. The fourth patient regarded it as merely an odd and rather amusing experience, in spite of a religious bias, which did not suffice to make her interpret it in terms of a divine experience. As already mentioned, however, this was not a typical ecstasy, and the feeling of merging with the cosmos was absent. This exhilarating experience is differently evaluated according to the individual personality.

Summary of Features of Personal Cases

Four cases have been recorded in which a special feeling of joy, a component of which was a sense of calmness, was experienced, associated with an alteration of consciousness which is typical of the states under consideration. This change involved an altered experience of the ego described as a feeling of merging with the cosmos or with God, although the personal identity did not become lost, but was rather intensified, particularly in one case, in striking contrast to her usual state. A change in time perception was also noted. The mood, the change in the experience of the ego, and the time-disorder were constant. The fourth case presented unusual features. The subjects retained a vivid memory of the states which in two cases effected a change in the subsequent personality of the patient.

Diagnostic Considerations

The first patient was an outspoken manic-depressive with obsessional and paranoid traits, with frequent hypomanic alternating with depressive phases, and with one ecstatic period. Hysterical features were not evident, though she tended to magnify her symptoms in order to obtain notice. This feature is of doubtful importance, as there were certainly no hysterical features similar to those in the other cases. The second case was one of recurrent depression with ecstatic phases and isolated hysterical conversion features. She had not a typical hysterical personality. She seemed in fact to be a serious and conscientious person. The third case was one of depression with ecstatic phases, with obsessional features and hysterical tinge. The fourth case was also one of recurrent depression, with one typical ecstatic interlude and occasional hysterical conversion features. The diagnosis in each case was based first on the family history, secondly on the previous personality, and in two cases on the occurrence of previous more or less circumscribed depressive attacks. Lastly the mental state during the present illness was taken into consideration. The family history in cases 1, 2, and 3 shows similar disorders. It may be noted that in the family history of two patients (2 and 3) there was a history of a depression of religious content, in case 2 the mother, in case 3 the sister. A history of obsessional illness was found in the family of the third patient.

Ecstasies differ from manic states. The essential nature of the ecstatic state lies in the remarkable pantheistic experience of the subject that he and the universe are one, associated with a mood which is quite peculiar and qualitatively different from that of mania. This mood is peaceful and tranquil, in marked contrast to mania. The difference between the two states was seen most clearly in the first patient, who, following a typical but mild hypomanic state, passed into the ecstasy and became less active, quieter, at peace with herself and everybody else. The paranoid features, usually intensified in mania, disappeared. Again in the third patient there was no pressure of thought, but she became rather more active than before. In the last patient there was happy tranquillity, in contrast to anything usually found in a manic state. The third case shows therefore that immobility is not an essential feature of these states, as Janet thinks, though there does exist a tendency in some states of ecstasy to a reduction of motor activity, as in case 1. It is possible that the decreased restlessness of this patient was merely a step towards a condition in which immobility was complete. With regard to the question of decreased motor activity, there is one condition, namely manic stupor, to bear in mind in considering the relationships of these states to others found in manic-depressive illness. It might well be that there is a relationship between manic stupor and the more extreme form of ecstasy. A study of Janet's case brings this to mind. Both manic stupor and ecstasy of the kind discussed here are rare. A difference between these two conditions is that in manic stupor there is usually "retardation" of thought and in the ecstasy an exuberant productivity. In Janet's case there was no flight of ideas. Those patients who in their stupor had a flight of ideas described this retrospectively, and did not refer to anything in the

nature of an ecstasy. It is not suggested that Janet's patient Madeleine presented a manic stupor, but a state more akin to hypnosis as evidenced, *inter alia*, by her heightened suggestibility. But Janet states that ecstatics should not be confused with somnambulists, whose mind is void and who have only one idea, that of obedience to the hypnotist. Further work on this problem of the possible relationship to manic stupor seems desirable.

The exalted manic who claims prophetic powers is familiar. This feature may be an expression of the increased feeling of power, but may also depend on the presence of a slight degree of that alteration of consciousness which characterizes ecstasy, just as in some depressives there are slight degrees of depersonalization which would pass unobserved unless careful scrutiny were made. The increased feeling of power also arises out of the peculiar affect—" Glücksaffekt "—as Mayer-Gross shows. Schou (1926) describes a case of manic-depressive psychosis in which the patient claimed to have been given special insight into the meaning of the Bible, which he felt he could interpret more clearly. Similar examples are common. The increased perception of detail may also be mentioned, although distractibility is absent. There is a difference in retrospective attitude of the manic and ecstatic patient. The manic patient regards his experience as something painful and to be forgotten. It is otherwise with the ecstatic patient, who often longs for the recurrence of the state of bliss, which he interprets as a rich spiritual experience and which may have a permanent effect on the personality. Jaspers quotes Gérard de Nerval as illustrating this attitude to mystical experiences. He goes on to say that this assimilation into the personality is predominantly but not exclusively the case in schizophrenic psychoses.

Janet shows the effect of his patient Madeleine's ecstatic experiences on her personality and how her subsequent attitude to the environment was changed—" the hospital was marvellous," " all the patients have features of a ravishing and angelic beauty, all the staff are so good to her, she has no difficulty with anybody." The difference in subsequent insight is probably not dependent on the mood alone. If it were, the retrospective attitude to a mania and an ecstasy might be expected to be the same. It is not dependent on the feeling of power, which is a feature of both. Janet interprets the attitude of the patient to the ecstasy on the basis that we associate sadness and misery with sickness, joy with well-being and success, and adds that it is necessary to understand that joy is not always reasonable. In writing so he addresses himself to the religious interpreters of ecstasy and not to psychiatrists. With reference to the influence of the conversion experience on the religious life, the character and personality of the individual are essential factors in determining how such states once experienced are interpreted by the subject. The intensity of the experience may also be a factor.

Starbuck (1909, p. 384) believed that the conversion experience brought about " a changed attitude towards life, which is fairly constant and permanent, although the feelings fluctuate. . . . " This is only true of some cases. I have recently seen two schizophrenics who had ecstatic or ecstasy-like experiences. One, a woman of 34, just before passing into a typical catatonic stupor, described

how two years previously she had become " changed " as the result of a " power outside herself." She felt " lighter " and the burden of sin was removed. She described it as " a nebulous idea of conscience, like a voice in the room, not necessarily conscience, but more directive than conscience." She heard the voice in her mind not in her ears, partly subjective, partly objective. She spoke of it as a " revelation." The other, a man of 34, who in the acute stages of his illness saw angels flying above the streets, the Devil in the form of sharks leaping from hedges, etc., described several " experiences of the Inner Light," as he termed them, which occurred during this period. Thus after animated discussion on religion one evening he returned home tired and lay on his bed. " The room became suffused with light (the electric light was on, but this was a spiritual not a natural light), enhancing the colours of the fabrics, etc. I was filled with a warmth and glow and a sense I was not alone." He had a similar experience after sending a religious tract to a sick woman he had heard of. He felt he might have been impertinent in this. " That same evening the ' light ' experience took place bringing conviction that this woman and I were mystically united in Heaven, and that what I had done was meeting with Heaven's approval." These experiences are different from those already described, though the passivity, intuitions, and sense of a greater power are present in all. These features of the ecstasy, however, are given characteristically schizophrenic mould and just as depersonalization occurs in different forms of mental disorder, so may ecstatic features, although it is doubtful if they ever take the form in schizophrenia which is found in the disorders under discussion here.

The relationship of other components of the morbid picture to ecstasy states may be mentioned. As already seen, three of the patients (2, 3, and 4) presented definite hysterical features. In Janet's case they were prominent, and it is assumed, probably too readily and on insufficient evidence, that all the noted mystics were hysterics. The question arises how far ecstatic states of the kind here described can arise on an hysterical basis alone, and how far on a manic-depressive alone. This is not easy to answer and can only be done on the basis of personally observed data. That a poor organization of the ego function is a feature of hysteria is admitted, and many of our most striking examples of depersonalization, such as micropsia, are found in hysterics without any notable degree of depression, though this last factor is often difficult to assess. Most, if not all of the examples of glossolalia and inspired writing occur in hysterics. The infectious religious movements almost certainly contain a notable proportion of such psychopaths, even allowing for mass suggestibility. That there is a relationship between the poorly integrated hysterical ego and ecstasy in at least some cases is undoubted, but it may be that as depersonalization is not peculiar to hysteria, neither is ecstasy. Certainly some of the more modern recorded experiences of " cosmic consciousness " do not appear to have involved hysterical personalities. The small total of psychiatrically observed material, however, makes conclusions impossible. The ecstasy may be related to the type of depersonalization occurring in obsessionals. Janet described Madeleine as a " scrupulous obsessional." Crichton-Browne reported a case in which attacks of loss of identity occurred after ruminations on such questions as

" Who am I ? " " What am I ? " etc. Obsessional features were found, notably in cases 1 and 3, but were not present in the other two. Janet (1903) sees a relationship between the two states and comments on the frequency with which he has found " sublime and solemn emotions " in these patients. On all these problems further work is required.

The third patient gave the most explicit information as to the circumstances in which the state arose. She had just been parted from her lover. Following this a period of painful tension of a peculiar kind arose and developed into the ecstasy. Those using dynamic interpretations will regard this as a compensation, a wish-fulfilment. Such a causal explanation cannot be invoked for her other ecstasies. In the second patient the ecstasy followed a period in which sense of guilt was strong. Janet regards these as reactions to a state produced by regression and withdrawal, and says : " they can in certain cases play the rôle of a defensive reaction which favours the gathering up again of forces and permitting later more complete action." Bleuler regards the ecstasy as the achievement of the maximum of wish-fulfilment. These states correspond to the obverse of the medal of which depersonalization is the reverse. Lastly, the age of the patient deserves consideration. None of the first three exceeded 30 years. The fourth, who is not directly comparable to the others, was 39. Manic states also tend to be more frequent in earlier life. With regard to conversion experiences, Starbuck (1909), as the result of a statistical enquiry, demonstrated that the large majority of religious conversions took place between the ages of 12 and 25 years. The first patient here was 24, the second 23, and the third 21 years when the ecstasy first appeared. It may also be noted that J. A. Symonds found these states recurred in him with diminishing frequency to the age of 28.

Summary

Four cases of affective disorder have been recorded in which ecstasy states occurred as phases. These cases have been recorded because little psychiatric study has been devoted to such cases owing to their comparative rarity. An attempt has been made to show the relationship of these states of ecstasy to affective disorders. The features in which the states described here resemble and differ from mania have been discussed. The characteristic manic mood differs widely from that found in ecstasy. The latter state comprised a sense of inner tranquillity and peace, a feeling of harmony with the environment, and in one case a reduction of motor activity in contrast with the previous hypomanic condition, and the paranoid attitude, which in this latter state had been prominent, disappeared. This reduction of motor activity also occurred in two other cases ; in the remaining case it seemed to be increased.

A difference in retrospective attitude towards the manic and ecstatic state was also observed, as well as the different effect caused by these states on the subsequent personality. A possible relationship between ecstasy and manic stupor is suggested and the desirability of further work on this problem indicated.

The relationship of other components of the morbid picture, the hysterical and obsessional, has been considered, but no conclusion has been reached. The difference between the ecstasies described here and those found in schizophrenia has also been briefly mentioned. Previous psychiatric observations on ecstasy have been discussed and criticized. The clinical features and the differential diagnosis have been discussed. A psychological causal interpretation of these states was not possible—a conclusion in agreement with Rümke (1924).

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CEREBELLAR SYNDROME IN AN ADULT WITH MALFORMATION OF THE CEREBELLUM AND BRAIN STEM (ARNOLD-CHIARI DEFORMITY), WITH A NOTE ON THE OCCURRENCE OF "TORPEDOES" IN THE CEREBELLUM

BY

C. D. ARING

From the Pathological Laboratory, National Hospital, Queen Square, London

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OBSERVATIONS are plentiful on congenital malformations of the nervous system which cause symptoms. The great majority of these studies, however, have been made in infants dying shortly after birth. It is of some interest to record a case of malformation of the cerebellum and brain stem, apparently congenital, which did not cause symptoms of a disabling nature until adulthood. This is the purpose of this paper. It is thought also that by calling attention to the histological changes in the cerebellum of this case that such changes may be removed from the category of the uncommon. It is possible that if careful search were made in the cerebellum of patients succumbing to the various "cerebellar system" diseases, structural changes of a similar kind would be found more often than is the case.

Case Report

J.P., a wood-worker, aged 20, was admitted to the National Hospital, Queen Square, on 30th August, 1935, under the late Dr. S. A. Kinnier Wilson.

The patient had always been well until 18 months before admission. At that time he noticed slight unsteadiness of the lower extremities, had difficulty in keeping his balance, and began to stagger on walking. There was a gradual increase in the severity of these symptoms and the progress of the disease during 8 months before admission. Three months before admission he had had bouts of sneezing, and at that time he could not swallow properly, for on several occasions fluid came back through his nose. There had, however, been no recurrence of these symptoms. At the time of admission to the National Hospital he said that he had difficulty in standing unsupported. Both legs were equally affected and he would stagger or fall to either side. He did not think the upper extremities were involved. There had never been weakness of any of the extremities. The patient had suffered from dull, frontal headaches for as long as he could remember, but they had not been incapacitating. The past history contained nothing indicating previous involvement of the nervous system or any incident that could be directly related to the condition of the patient at

the time of entrance to the hospital. The history obtained from the patient and from the parents revealed no instance of nervous or mental disease in any of his family.

On examination he was found to be somewhat slow mentally and he co-operated poorly. His speech was rather slow and slurred. There was a coarse horizontal nystagmus on looking upward or to the right, while on looking to the left the nystagmus was more rapid and not so coarse. The left side of the palate arched on phonation rather more than the right, indicating a slight weakness of the right side of the palate. The right sternomastoid and trapezius muscles were not so well developed or as powerful as those of the left. There was a fascicular tremor throughout the tongue musculature. The head was tilted slightly toward the right shoulder and there was a fine tremor of the head. Apart from these findings the functions of the cranial nerves and the special senses were normal. A pes equino-cavus deformity of both feet was noted. No alteration of development or motor power of the extremities was observed, but there was a generalized increase in muscle tone, more obvious in the lower extremities. A coarse fascicular tremor was present in the muscles of the left extremities. There was a fine tremor of the outstretched hands, and finger to nose tests were performed with a moderate terminal tremor. Rapid alternating movements of the hands were slow and " toe-wiggling " was poorly performed. Placing the heel on the knee, then directing the great toe towards the examiner's finger, was performed with moderate ataxia bilaterally. It was evident that spasticity and ataxia rather than weakness were the cause of the disability. The gait was very ataxic ; the patient walked slowly and stiffly on a wide base and with his gaze fixed on the ground. Closure of the eyes greatly increased the unsteadiness. All of the tendon reflexes were very brisk; knee and ankle clonus was obtained bilaterally. The abdominal reflexes were normal and the plantar responses were extensor in type. The patient occasionally failed to identify passive toe movements, otherwise there was no sensory abnormality. The general physical examination was entirely normal.

A lumbar puncture performed on 31st, August 1935, gave a clear fluid under normal pressure. There were 2 cells per cm., a total protein of 0·22 per cent., and strongly positive globulin reactions. Lange's gold sol test was normal and the Wassermann reaction was negative in both the cerebrospinal fluid and the blood.

The patient was at first thought to be suffering from spino-cerebellar ataxia. He commenced to exhibit a peculiar mental reaction, becoming morose and occasionally very belligerent and abusive. The nystagmus continued to be slower and coarser on looking to the right. This fact, together with the high protein content of the cerebrospinal fluid, suggested the possibility of a right cerebellar cyst. On 13th November, 1935, a bilateral ventricular tap was performed and the withdrawn fluid replaced by air. The ventricular fluids were entirely normal and contained 0·01 per cent. of protein. The ventriculograms were also normal. On 3rd December, 1935, a cerebellar exploration revealed nothing of note besides marked herniation through the foramen magnum of the tonsils of the cerebellum, which were attached tightly together by adhesions in the arachnoid. There was no increase of intracranial pressure. The arch of the atlas was removed in order to liberate the tonsils, which even then were difficult to mobilize, as they reached down to the axis. The right cerebellar tonsil was somewhat larger than the left and the vermis was displaced slightly toward the left. The arachnoid at the lower end of the vermis and between the tonsils was considerably thickened. The adhesions between the tonsils were broken down with difficulty, after which the lower end of the fourth ventricle and the medulla could be seen. Exploration of the cerebellar lobes revealed no tumour. The patient recovered consciousness shortly after the operation had been completed and recognized individuals. Several hours later the pulse quickened and he developed Cheyne-Stokes respiration and cyanosis. His temperature was subnormal. He gradually became worse, the pulse becoming feeble and more rapid, and death occurred on 4th December, 1935, eighteen hours after operation.

Pathological Findings

A necropsy was performed two hours after death and the brain and cord were removed. Several abnormalities were visible to the naked eye. Both tonsils of the cerebellum passed downward over the dorsal surface of the medulla, to which they were firmly attached. The appearance was not that of a cerebellar pressure cone, as the right tonsil lay unusually far dorsally and seemed to be somewhat enlarged. The dome of the cerebellum lay asymmetrically, the highest point being to the left of the midline. The most rostral portion of the medulla appeared unusually thin and soft, so that the brain stem tended to bend abnormally at this level. No cause for death and no hæmorrhage at the site of operation were found.

Pieces from each spinal segment, from various levels of the brain stem, and from different parts of the cerebellum and cerebral cortex were examined by several histological methods. The Weil, Weigert-Pal and Mallory's phosphotungstic acid hæmatoxylin methods were applied to the brain stem and to the spinal cord. A moderate degree of degeneration was present in the anterior and posterior roots, especially in the cervical region. These stains revealed definite demyelinization in the cord affecting rather diffusely the anterolateral tracts. In the cervical region the dorsal and possibly also the ventral spino-cerebellar tracts were spared to some extent. There was some demyelinization and fairly intense neuroglial sclerosis in the columns of Goll from the third cervical segment upward and slighter neurolgial overgrowth at lower levels of the cervical cord. There was some distension of the central canal of the cord at the levels of cervical segments six, seven, and eight. This was lined only partly on its ventral surface by ependyma and reached but did not penetrate the base of the dorsal horn on either side. The ventral portion of the medulla was shrunken and distorted throughout. At the caudal level (Fig. 1, E) the medulla was flattened in its antero-posterior diameter despite the very obvious prominence of the dorsal columns. The column of Goll projected dorsally outwards from the columns of Burdach, resulting in an abnormal outline of the medulla at this level. At a slightly higher level (Fig. 1, D) there was a rather deep indentation of the white matter of the medulla just ventral to the nucleus of the spinal root of the trigeminal nerve, which dislocated the dorsal spino-cerebellar tract somewhat in a ventral and medial direction. At a level about half-way up the medulla the olives and restiform bodies were greatly shrunken, so that the whole transverse diameter of the medulla was abruptly reduced and the width on cross-section was greatly narrowed. The cells of the olives in this area were shrunken and stained darkly and were very irregularly spaced in the foliæ as though many had disappeared. There was considerable gliosis in the hilum of the olives. The olives although much shrunken remained visible up to the junction of the medulla and pons. At about the level of the middle of the inferior olives (Fig. 1, C) one observed besides the distortion and shrinkage that the calamus scriptorius was overhung more on one side than the other by the inferior medullary velum and a cleft was formed to one side, running a short distance into the grey matter of the floor of the ventricle in this region.

At the upper level of the medulla (Fig. 1, B) there was comparatively little distortion besides pinching of the ventrolateral margins, but there was obvious reduction in the size of all structures in this area. The pons as a whole was shrunken, especially in its caudal two-thirds. The pinching of the ventrolateral margin was very obvious in the caudal part of the pons and the transverse fibres were very pale in the caudal one-third of the pons.

Various staining methods (Mallory's phosphotungstic acid hæmatoxylin, hæmatoxylin and van Gieson, silver counterstained with thionin) applied to the cerebellum revealed no abnormality. There was no dropping out of Purkinje cells and no evident loss of fibres ; the roof nuclei and other structures in the cerebellum appeared entirely normal. However, when the Gros method for silver impregnation was utilized and the reduction in ammonium silver nitrate allowed to proceed until the axis cylinders of the Purkinje cells had taken the stain fully (to the detriment of the medullary parts of the cerebellum), it was seen that practically all of the individual axones of the Purkinje cells contained a bulbous swelling sometimes called a " torpedo " (Fig. 2). Under high magnification the fibres of the baskets surrounding the Purkinje cells could be followed into the granular layer as they travelled along the Purkinje axones to envelop the " torpedoes." These bulbous swellings of the Purkinje axones were generalized throughout the cerebellar folia in the same profusion as illustrated in the photograph. No abnormality was found in the cerebral cortex.

In summary a man aged 20 began to complain of unsteadiness in the lower extremities 22 months before death. There was gradual progression until 18 months later, when he had difficulty in standing unsupported and the gait was staggering in type. Examination 4 months before death revealed mental changes, nystagmus, and hesitant speech. There was increased muscle tone in all of the extremities. The gait was very ataxic. The tendon reflexes were extremely brisk and the plantar responses were extensor in type. Sensation was practically intact. The cerebrospinal fluid was normal except for a great excess of protein content. His status remained unchanged for nearly four months. Death occurred after cerebellar exploration. Necropsy revealed adhesions between the elongated cerebellar tonsils, both of which were adherent to the medulla. The medulla was small and deformed, chiefly because of " wasting " in the region of the olives and of the olives themselves in the rostral half of the medulla. The caudal part of the pons was shrunken and there was a loss of transverse fibres in the pons. The pyramidal tracts and spino-cerebellar tracts in the cord were somewhat degenerated in the lower levels and approximated to the normal in the higher sections of the cervical cord and medulla. There was moderate degeneration in the columns of Goll. In the cerebellum numerous " torpedoes " in the axones of the Purkinje cells were found.

Discussion

As the case appears to represent several of the characteristics found in the Arnold-Chiari deformity (Arnold (1894), Chiari (1891, 1896), Parker and McConnell (1937), Russell and Donald (1935), Schwalbe and Gredig (1907)), it will be helpful to outline the several findings which have led in the past to a diagnosis of this deformity.

The Arnold-Chiari deformity has been described in a fœtus and in a subject of 68 years of age. Clinical symptoms and signs recorded in the literature include those commonly found in association with disturbance of pyramidal function and with hydrocephalus. It has not been possible to trace any record of a case presenting symptoms and signs of a cerebellar syndrome. Through the kindness of Coburn and Penfield (1938) I have been informed of a case which they are reporting elsewhere. This is a case of a female patient aged 29 years. During childhood she had an operation for the repair of a thoracic spina bifida. Later she developed a tendency to fall forward occasionally. This, along with a horizontal and vertical nystagmus, suggested some cerebellar abnormality, for which she was explored. Two months later she died.

Pathologically the most obvious abnormality of the nervous system with the Arnold-Chiari deformity is an elongation of the tonsils and inferior portion of the cerebellum, so that these parts may extend downward for varying distances into the spinal canal. The pia arachnoid covering this malformation is usually thickened and may cause the prolongations of cerebellum to be adherent to the brain stem. Hydrocephalus and spina bifida are usually but not always present. The pons and medulla are commonly noted to be flattened or bent or asymmetrical and occasionally lack the ventral protuberance. Hypoplasia of the cerebellum and pons have been observed in cases of the Arnold-Chiari deformity. Hydromyelia of the cord has sometimes been found. No very satisfactory microscopic study of the nervous system has been performed to date. Examination of the elongation of the cerebellum has revealed sclerosis in some cases and normal cerebellar convolutions in others.

The pathology of the present case corresponds in a general way to that which has been previously described for the Arnold-Chiari deformity. The elongations of the cerebellum and the cohesive pia arachnoid found at the operation and again at autopsy are rather typical. The small pons and deformed medulla found in this case are in keeping, and shrunken olives have been noted in Chiari's (1891) descriptions. In some of his cases Chiari recorded abnormalities of the olives, which ranged from " olives placed with their longitudinal axis oblique " to complete absence of the olives in one case. There was no spina bifida in this case, but no special search was made for it ; nor was there any hydrocephalus.

The possibility that this case might represent one of the variants of spinocerebellar ataxia (Chart 1) must be considered. " Hereditary cerebellar ataxia," the title which Marie (1893) advanced for the cases with primary involvement of the cerebellum, was the result of the collation of the cases of other authors. As Holmes (1907) has pointed out, the cases collected by Marie for inclusion under this title were dispersed by anatomical examination of the nervous systems of

these individuals. Despite this fact, the heading " Marie's hereditary cerebellar ataxia " remains a common one. It is well to dispense with the term and to list the cases where they belong, either under the heading of primary parenchymatous degeneration of the cerebellum (Holmes, 1907) or olivo-ponto-cerebellar atrophy. Of the various forms of spino-cerebellar degeneration this case most nearly resembles olivo-ponto-cerebellar atrophy. The age of onset in olivo-ponto-cerebellar atrophy commonly commences late in life, usually in the sixth decade. Mental symptoms are not uncommon in this form, and except for these features it is doubtful if any clinical differentiation is possible. In olivo-ponto-cerebellar degeneration the inferior olive and middle peduncle are the structures most frequently and severely involved, as they were in this case. Degeneration of the long tracts of the spinal cord has been recorded in olivo-ponto-cerebellar atrophy. In the present case the diffuse degeneration of the antero-lateral tracts and the degeneration of the posterior columns of Goll in the upper cervical region were of sufficient severity to cause clinical signs.

CHART 1

	FAMILIAL ATAXIA (Freidreich)	OLIVO-PONTO-CEREBELLAR ATROPHY (Dejerine and Thomas)	SUBACUTE SPINO-CEREBELLAR ATROPHY (Greenfield)	PRIMARY PARENCHYMATOUS DEGENERATION OF THE CEREBELLUM (Holmes)
Hereditary or familial history	+	0	0	+
Age period at onset	Juvenile.	Old.	Adult to old.	Adult.
Mental signs	±	+	++	0
Cerebrospinal fluid	A few early cases may have a slight increase in cells and protein. Occasionally changes in the Gold curve and a slightly positive Wassermann (without syphilis).		Intense cellular reaction and marked increase in the protein. First and second zone changes in the Gold curve.	Sometimes excess of protein and globulin and changes in Gold curve. (Parker and Kernohan (1933).)
Pathology in :				
Optic nerve	±	0	0	±
Nucleus of Luys	0	0	+	0
Pons	Small.	+	0	0
Olive	0	+	0	+
Spinal tracts	++	±	++	0
Cerebellum	±	+	++	++

+, usually present. 0, usually absent. ±, may or may not be present.
++, severe involvement.

Although the white matter of the cerebellum showed no evident loss of fibres the presence of " torpedoes " indicates that this was beginning. The occurrence of numerous " torpedoes " in the cerebellum is never a common

finding and was one of the most striking features in the pathology of this case. These swellings of the axones of the Purkinje cells were the only pathological findings in the cerebellum. In olivo-ponto-cerebellar atrophy as described by Dejerine and Thomas (1900), the cortex of the cerebellum atrophies. However, cases have been reported in which the inferior olive and nuclei pontis were atrophied without any evident degeneration of the cerebellum and others in which the olives were degenerated with little or no degeneration of the pontine nuclei or middle peduncles and with involvement of the dentate nuclei.

Olivo-ponto-cerebellar atrophy is probably the commonest and most clear-cut entity of the spino-cerebellar ataxias, but even in this sub-heading (Chart 1) many intermediate and transitional states exist, one of which might be represented by this case, which it would be difficult to classify with any of the other well-known types of spino-cerebellar degeneration. A glance at Chart 1 will readily corroborate this statement and accordingly curtail the discussion. The rapid onset of cerebellar symptoms in early adult life in this case is indeed an unusual phenomenon, for which the cause remains unexplained. It would appear to be comparable with the onset in Coburn and Penfield's case (aged 29 years) and with the onset of hydrocephalic symptoms in Parker and McConnell's cases (aged 10, 18, and 32 years) of the Arnold-Chiari deformity.

" Torpedoes " in the Cerebellum

Sections from the cerebellum of neurological cases selected at random were subjected to the Gros method for silver impregnation. " Torpedoes " were found in moderate numbers in two cases of olive-ponto-cerebellar atrophy and in a case of granular ependymitis. In the former there was a great loss of Purkinje cells and the baskets appeared disintegrated. Where a " torpedo " was found one could trace the axone centrifugally up through the basket fibres to a Purkinje cell. In the case of granular ependymitis there was no loss of Purkinje cells and the cerebellum appeared otherwise intact. In none of these cases did the " torpedoes " appear in anywhere near the numbers seen in the cerebellum of the case reported in detail (Fig. 2). Rare " torpedoes " were found in the cerebella of individual patients succumbing to dementia paralytica (Fig. 3), syphilis of the central nervous system with granular ependymitis and atrophy of the left cerebral hemisphere with convulsive seizures, and of two patients with amaurotic family idiocy (Tay-Sachs). In this group of cases it was usually found that the Purkinje cell whose axone was involved exhibited no visible abnormality. No " torpedoes " were found in the cerebella of the following single cases : syphilitic myelitis with syringomyelia, tabes dorsalis, neuromyelitis optica, post-encephalitic Parkinsonism, acute chorea, disseminate sclerosis, old cerebral contusion, amaurotic family idiocy (Bielschowsky type), cerebellar abscess, and cerebellar agenesis. Neither were they seen in four cases of dementia paralytica.

This round or spindle-shaped and usually homogeneous swelling incorporated along the course of the axone of the Purkinje cell has been noted by other workers in cases of dementia paralytica, in diffuse atrophies and localized

disease of the cerebellum, in tuberous sclerosis, dementia præcox, familial ataxia (Friedreich), amaurotic family idiocy, and in olivo-ponto-cerebellar atrophy. Bielschowsky (1920) looked upon this axone swelling as a " trivial reaction phenomenon " and Spielmeyer (1922) noted that this swelling might be a primary injury of the axis cylinder due to all sorts of acute and chronic causes.

This change is present in varying degree in cerebella where no other abnormality is found and in cerebella with other marked anatomical changes. An attempt to connect this individual pathological change with neurological dysfunction would be speculative. I have been unable to find the report of a case of swelling in the axis cylinders of the Purkinje cells of the cerebellum without change elsewhere in the central nervous system.

Summary

A case is described of a man aged 20, who died 22 months after the onset of symptoms and who presented many of the pathological findings of the Arnold-Chiari deformity. The history was one of progressive ataxia of the lower extremities. Mental changes, nystagmus, hyperactive tendon reflexes, and extensor plantar responses were also present. There was an excess of protein in the cerebrospinal fluid.

Pathologically the following abnormalities were found : a small deformed medulla with degeneration of the olives in the rostral one-half of the medulla, reduction in the size of the pons with degeneration of the transverse fibres, especially those in the caudal one-third of the pons, degeneration of the spino-cerebellar and pyramidal tracts in the lower levels of the spinal cord, and moderate degeneration in the columns of Goll and in the anterior and posterior roots of the upper segments of the cervical cord. The cerebellum was intact except for the presence of a bulbous swelling (" torpedoes ") in a great many of the axones of the Purkinje cells.

The presence of " torpedoes " in moderate numbers in the axones of Purkinje cells was found in cases of olivo-ponto-cerebellar atrophy and granular ependymitis. Occasional " torpedoes " were observed in cases of dementia paralytica, syphilis of the central nervous system, atrophy of one cerebra hemisphere, and amaurotic family idiocy (Tay-Sachs).

I am indebted to Dr. J. G. Greenfield for his helpful guidance. This work was carried out during the tenure of a Rockefeller Fellowship.

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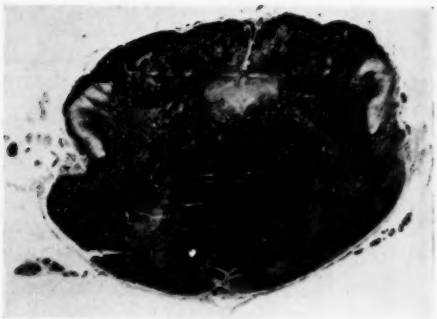
A

B



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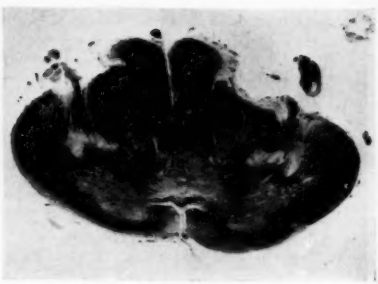


E

Fig. 1.—Sections from various levels of the brain stem to illustrate the distortion and shrinkage of the ventral half of the medulla. Weil method for myelin sheaths. Magnification the same throughout this series : ×6·75.

Fig. 2.—A photomicrograph indicating the profusion of " torpedoes " in the axones of the Purkinje cells of the cerebellum in the case of Arnold-Chiari deformity of the brain stem described in the text. Gros method for silver impregnation.

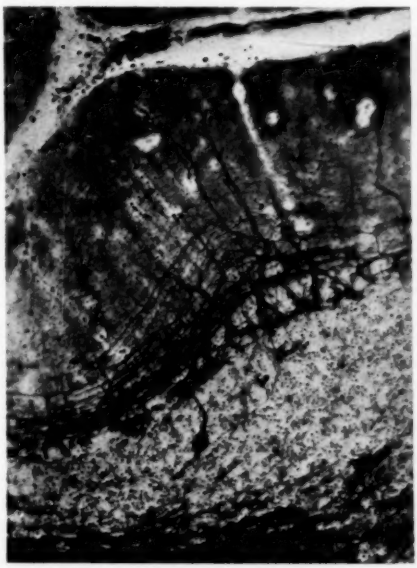


Fig. 3.—A " torpedo " in the cerebellum of a case of dementia paralytica. Gros method for silver impregnation.

MENTAL DISORDER IN CUSHING'S SYNDROME

BY

W. S. MACLAY AND A. B. STOKES

Pathological report by D. S. RUSSELL

From the Maudsley Hospital and Bernhard Baron Institute of Pathology, The London Hospital

(RECEIVED 16TH FEBRUARY, 1938)

RESEARCHES into endocrine function and dysfunction have thrown new light on many clinical conditions, and great hopes have been aroused that obscurities of causation may ultimately be traced to an endocrine source. The obvious relationship between certain emotional states, e.g. fear, and the activity of certain endocrine glands, e.g. suprarenals, suggested that such an approach might be specially valuable in psychiatry; nevertheless, the specific association of a given mental disorder with a given endocrine state has not been accepted and has fallen into disrepute. Perhaps because of this certain aspects of endocrine disorder have not been sufficiently stressed.

An endocrine disorder may be related to an abnormal mental state in the following ways: (1) Both the endocrine and mental illness may be expressions of an underlying cause, either of a pathological genetic disposition or an environmental noxa. (2) The endocrine disorder may precede and be the immediate cause of disturbed function in the brain. (3) The abnormal mental state may precede and be the cause of abnormal endocrine function. (4) The endocrine disorder may produce certain systemic disturbances which secondarily involve the brain structure and disturb its function. (5) The endocrine disorder may produce bodily changes of social significance so great that the personality shows signs of stress. These relationships, easily differentiated in theory, are in practice obscure, and the obscurity is made greater by the possibility of vicious circles in which the endocrine and neural factors influence one another successively.

In considering the mental states associated with Cushing's syndrome, the fifth and fourth categories of relationship, as made above, are of obvious importance. The social consequences of this syndrome in any patient are tremendous, but particularly so in females. Obstinate hirsuties, adiposity, and disturbances of sexual function are outstanding as social obstacles to which the patient has to make a new adjustment. Again, owing to metabolic changes, hypertension, arteriosclerosis, possible cardiac and renal failure, etc., the adjusting mechanism can itself become impaired and this impairment may

become manifest as a change of personality. In these circumstances it would be surprising if symptoms of mental illness, of greater or lesser degree, were not present in a large proportion of patients. However, out of 49 cases in the literature of Cushing's syndrome, including tumours of the suprarenal cortex and thymus, the mental state was mentioned in only 20. It is unnecessary to give full references to the literature of Cushing's syndrome, as it has recently been well reviewed by Pardee (1937), who gives 152 references. The main abnormal findings were stated as follows :—

Fatigue	mentioned in	4 cases
Self-consciousness	,,	4 cases
Mental dullness	,,	3 cases
Anxiety symptoms	,,	3 cases
Depression	,,	3 cases
Irritability	,,	2 cases
Memory upset	,,	1 case
Dreams and visions	,,	1 case
Lack of concentration	,,	1 case
Lack of interest	,,	2 cases
Euphoria	,,	1 case
Delusions	,,	2 cases
Confusion	,,	2 cases

In such reports, the mental status was, with few exceptions, only referred to in casual sentences or short paragraphs from which the above data were compiled, but from their content there was clear evidence of the presence of a mass of interesting psychiatric material which had been disregarded.

The following case illustrates the development of a psychosis in a victim of this disorder, in whom the opportunities for observation and investigation were exceptional in that she was under medical care during nearly the whole of her illness, and was in hospital with daily observation for the last two years of her life.

Personal Case

Female, æt. 29 years. Was admitted to hospital in May 1935 because of two suicidal attempts following a period of depression and change of personality. She was under observation in hospital until her death in April 1937.

Her father, æt. 75 years, and mother, æt. 64 years, are alive and well. The father has been married twice, having one daughter by his first marriage and two sons and four daughters, of whom the patient is the second, by his second marriage. The family life has been happy and normal. There is no history of any nervous, mental, or endocrine illness among the relatives.

Her early development was uneventful. She did well at school, where she matriculated and won a scholarship. She enjoyed her school life, liked games and was good at them. Since then she has worked efficiently as a clerk for four years in one post and nine years in another, earning fifty shillings a week. She worked until one week before admission to hospital. Menstruation started at 16 years and was regular and normal until the onset of her illness. Her health has been good except for an attack of influenza in 1918. There is no history of any previous mental illness. Her previous personality has been good. Her friends often called her placid and carefree. She got on well with her family and friends, although in her own opinion she was inclined to be shy and sensitive. She played a lot of games, attended evening classes, and was fond of reading. She was never jealous and never worried about her health. Her appearance was attractive, as shown in the photograph (Fig. 1).

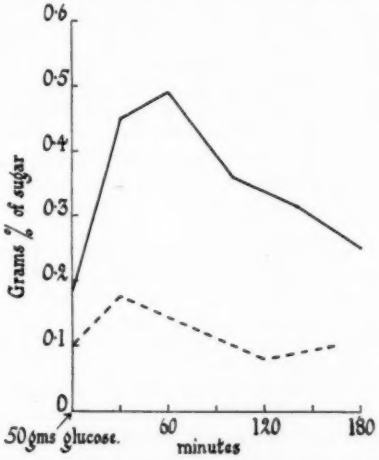
She was perfectly well until August 1933, when she developed amenorrhœa. From then until her admission she only menstruated on three or four occasions, the flow being very scanty. About the same time she showed excessive growth of hair on the face, some brown pigmentation, and severe pain in the lower abdomen. She was admitted to a hospital in March 1934 for the above complaints, where investigations revealed only an irregular glycosuria. In November 1934 she complained of spots in front of her eyes and pain with tenderness on the left side of her face. During the latter part of 1934 and in 1935 there was a gradual but marked change in her personality. She became seclusive, refusing all social engagements ; she became morbidly sensitive about the hair on her face ; she became jealous of her sister and of any new clothes that her sister bought. She gradually lost interest in everything, could not concentrate, and became depressed. For some months before admission she felt hopeless and had fits of weeping. She would wake up at night and cry, " Why can't I die ? " and on one occasion tried to throw herself out of the window. She was able to continue work until May 1935, but was found one day to have inflicted superficial wounds on her wrists with a razor. She was admitted to an observation ward from which she was transferred to the Maudsley Hospital.

She was restless, self-concerned, and unhappy, but discussed her illness intelligently. Her mood was one of bitterness against the world, and she attributed her depression to worry about her appearance and the apparent inability of any doctor to cure her. She thought that all her symptoms might be due to anæmia. She was insistent that she had no desire to live unless cured. There were no delusions or hallucinations ; she was correctly orientated ; her memory showed no apparent defect, though she herself thought that it was bad. Her grasp of general information was good, but she showed poor powers of concentration and had a real difficulty in doing an arithmetical test, such as subtracting serial sevens. Her insight was poor and she seemed unwilling or unable to understand a simply worded explanation of her illness. She would accept reassurance temporarily, but asked all the same questions again on the following day. Her chief complaints were of nausea and anorexia, hair on the face, and pain in the region of the left temple. On questioning her she had many other symptoms, namely, amenorrhœa, blurring of vision, with black spots in front of her eyes, backache, shooting pains in the lower abdomen, and a feeling of fatigue and weakness which she described by saying, " I used to walk quickly ; now I amble along." Most of the above symptoms persisted during her stay in hospital.

She was a well-built woman with a tendency to adiposity of the face, neck, and trunk, but not of the limbs. The face looked congested and plethoric, while the limbs showed a " cyanotic " appearance. There was marked hypertrichosis affecting the face, body, and limbs, especially the face, where the hair on the upper lip and chin was curly and grew rapidly, requiring frequent shaving or pumice-stone treatment to control it (Fig. 2). She bruised easily and even without injury small ecchymoses often appeared on various parts of her body. At one stage of her illness numerous petechial spots appeared on both breasts. The visual fields were normal. Ophthalmoscopic examination showed no abnormality. The blood pressure, which was recorded at frequent intervals, was always raised and was about 180 systolic and 110–120 diastolic. The left ventricle was enlarged and the aortic 2nd sound accentuated.

The laboratory findings were as follows : (1) Blood : (*a*) Complete blood examinations were made at intervals, but never showed any tendency towards polycythemia or any marked variations from the example given. Red blood corpuscles, 4,440,000 ; white blood corpuscles, 6,000 ; hæmoglobin, 14·3 gm. ; colour index, 1·0. Size, 7·2 μ. Differential count : polymorphs, 4,260 ; lymphocytes, 1,500 ; hyaline, 180 ; basophils, 60. (*b*) Blood urea, 21·2 mg. per cent. (*c*) Serum calcium, 10·0 mg. per cent. ; serum potassium, 15·0 mg. per cent. ; serum sodium, 226·0 mg. per cent. ; phosphatase, 0·274 units. (*d*) Coagulation time=3 minutes (Sabraze's Method). (*e*) W.R. negative. (*f*) Fasting blood-sugar level was always very high (Calvert's modification of Folin and Wu), as shown in graph of blood sugar curve. (2) The

cerebrospinal fluid was normal when examined on two occasions. (3) Basal metabolic rate, +19 per cent. (Benedict's method); impedance angle, normal. (4) Zondek Ascheim test, negative. (5) Urine consistently showed a high specific gravity and much sugar except when insulin was being given. In spite of the large quantities of sugar, up to as much as 5·0 gm. per cent., there were never any ketone bodies in the urine. Traces of albumen only appeared when the urine was infected. The glycosuria was easily controlled by 10 units of insulin twice a day. A urea clearance test done in August 1935 was the only indication that the kidneys might not be acting efficiently. Urea clearance test: blood urea, 21·2 mg. per cent. After first hour, 64·5 per cent.; after second hour, 26·0 per cent. (6) X-ray appearances: The skull and pituitary fossa were X-rayed on four occasions without showing any abnormality; the last



photograph showed the decompression opening (referred to later) and the radon seeds, one of which was in the pituitary fossa. Radiographs of the long bones and spine were normal on admission, but a year later definite osteoporosis of the spine was seen. Radiographs of the chest showed an enlarged left ventricle of the heart. There was no evidence of an enlarged thymus.

In September 1935 a course of deep X-ray therapy directed at the pituitary gland was commenced, but had to be interrupted after two treatments owing to the patient falling in the ward and striking the right side of her head on the floor. This was followed by papillœdema, thrombosis of the central vein of the retina, and numerous retinal hæmorrhages in the right eye. The condition improved slowly, but left her with marked defect of vision in the right eye. The left eye was not affected. In December 1935 a laparotomy was done and an appendix which showed signs of chronic inflammation both by naked eye and microscopic examination was removed. The surgeon reported that the uterus was infantile, the ovaries both very small, and that nothing abnormal could be felt in the region of the suprarenal glands. Two days after the operation she suddenly became unconscious and remained so for two days, the condition being suggestive of a small cerebral embolus. From this she made a good recovery. Up to this time she had shown increasing self-concern and depression, remarking on several occasions that she would commit suicide if it were not for the trouble to others which such an action would cause. At the beginning of 1936 her mood seemed to vary with the pain in the left temple. When free from this pain she was up and about, behaving in a cheerful, sociable way with the other patients, but about March she became worse again, was very preoccupied with her ailments, and

for the first time began to express morbid ideas about her bodily state, saying, " I'm certain there is something wrong with my bowels " or " I'm sure there is something behind my eye."

The course of deep X-ray therapy was recommenced and completed without any untoward effects, except loss of hair from the parts of the head irradiated. By May she was the picture of misery ; delusions had developed and were characterized by feelings of self-reproach. She would ask if she was a " bad woman " of if she was really a thief or if she had committed some crime. She had vague ideas that her amenorrhœa might be connected with pregnancy. She was suspicious and rather bewildered ; she thought there might be a dictaphone in the room to spy on her and had the feeling at night that there was play-acting going on in the ward, and that the whole of her life was re-enacted. She took her food poorly and lost nearly a stone in weight.

In June 1936 it was decided to explore the pituitary fossa. Mr. Hugh Cairn's operation note is as follows : " The pituitary was approached via the right transfrontal route without any special difficulty, in fact, more easily than usual, because when the dura was opened the subarachnoid space was found to be greatly distended with fluid all over the right frontal region. The cortex itself, however, did not appear to be shrunken or atrophic. The exposure of the pituitary was technically very difficult, though division of the right optic nerve helped a little. A small gland in a small sella was seen and it was possible to insert two radon seeds. She recovered from the operation satisfactorily."

After the operation there was little change in her mental state. She was still restless and uncertain and needed constant observation. She admitted that her headaches were a little better, but was concerned about her eyesight. She was now quite blind in the right eye and had a left temporal hemianopia. She was sent as a voluntary patient to a mental hospital in October, 1936. During the remainder of her illness she was at most times self-reproachful, deluded, and impulsive. Ideas of reference were marked, she thought that she heard people say " that woman " in a scornful way, and felt that her name was coupled with unpleasant things. She thought that she was accused of theft and that people avoided her. Sometimes she was noisy, laughing, talking, singing, and trying to run away. Occasionally she was confused, but often it was possible to get her to talk coherently and to discuss her illness, though she constantly reverted to her delusions. The degree of blindness in the left eye increased with the development of marked optic atrophy. It was difficult usually to get her to take her diet, excepting at the period shortly before her death, when she ate voraciously. She had increasing thirst, which was never satisfied. She died in April 1937.

Discussion

The post-mortem findings are described and discussed in the appendix, but even without them the clinical picture is highly suggestive of Cushing's syndrome. The symptomatology conforms closely to the requirements laid down by Cushing, including as it does weakness, fatigability, backache, abdominal pains, aching pains in the eyes, retinal hæmorrhages, ecchymoses, pigmentation, plethoric appearance of skin, abnormal hirsuties, adiposity of face and shoulders, sexual dystrophy, vascular hypertension, osteoporosis, hyperglycæmia, polyphagia, polydipsia, and susceptibility to pulmonary infection. Cushing (1932) himself recognized that the syndrome is polyglandular ; and a polyglandular syndrome is apparently nothing more than a group of secondary functional alterations occurring in the ductless gland series whenever the activity of one of the glands has become primarily affected. It may, however, be impossible

to determine clinically where the primary fault is located. Lescher and Robb Smith (1935), after a careful comparison of the pituitary basophilic syndrome and the adrenal cortico-genital syndrome, say : " It must be concluded that Cushing's syndrome, complete in its entirety, may be caused by such diseases as tumours of the adrenal cortex, and so a clinical distinction cannot always be made between them."

The difficulties of establishing the nature of the relationship between the endocrine state and the mental disorder are illustrative of the difficulties always arising in this field. The hyperthyroid state is associated clinically with anxiety and irritability ; the cretin has been described as showing psychic and motor retardation, not infrequently accompanied by obsessional features ; pancreatic tumours have been associated with neurasthenic symptoms of widely varying nature ; hypoparathyroidism has been complicated by hallucinatory experiences ; gonadal pathological changes have been described in schizophrenia, etc. In regard to pituitary disorders Birnbaum (1930) says : " The mental states accompanying anomalies of function or disease of the hypophysis should be regarded with special reserve. First, some of these pituitary disorders are still debatable in their pathological interpretation, and secondly some of the observations are based on tumours which produced signs of increased intracranial pressure." Kraepelin and Lange (1927) after describing some of the mental changes which may accompany acromegaly go on to say : " Furthermore, in acromegaly psychoses can be observed that are in no close relation to the physical disease . . . it is most likely in such instances that there is only an incidental combination which is favoured by a common predisposition " ; or again, after mentioning the wide variety of mental disturbances which can occur with Frohlich's syndrome, they say : " It is an open question how far these observations point to a causal relationship to the hypophysical disease ; it is most likely for the confusional states and for the dementia and somnolence which can be observed in the later stages of the disease." Such relationships as have been described are complex and as difficult to elucidate as in the present case. Hoskins (1934) sums up the position when he says : " Psychoses may be importantly determined by antecedent or concurrent endocrine abnormality, but none of the evidence compels that conclusion."

The first evidences of ill health in this patient were physical complaints, amenorrhœa, changed appearance, hypertrichosis, pain in head and abdomen, of such a character as to make the change of personality which followed easily comprehensible in the early stages of her illness as an emotional reaction to her realization of them. It is not hard to understand how a girl of her age, appearance, and personality could become jealous of her sister's good health, seclusive and morose on account of her changed appearance, irritable in view of the pain which she suffered, and later depressed when she found that no one seemed capable of doing anything to alleviate her condition. As the illness progressed, however, other factors, as mentioned at the beginning of the paper, and more particularly the physiological abnormalities, came into greater prominence, and more and more clearly could be seen reflected in the psychological picture. Of these the most obvious were changes which occur frequently in hypertensive

states, such as loss of the elasticity and adaptability of the personality in regard to all mental processes, the exaggeration of psychological features which were present before but either latent or less manifest, and depression with paranoid delusions and periods of confusion, panic, or excitement. This corresponds closely to the descriptions of psychoses in hypertensive states by such writers as Krapf (1937) and Meyer-Gross (1937). Other physiological disturbances must also exert an influence on the mental state, but in the present state of knowledge their effect cannot be assessed. In our case, no straightforward causal relationship between endocrine disorder and psychological symptomatology can be demonstrated. The features in evidence are the great emotional stress to which the patient was subjected, the change of personality, and the onset of a psychosis. The early symptoms are easily understood as a psychological response ; the final symptoms are definitely of an organic kind, due to systemic disturbances which finally involved the brain and disturbed its function. It is, however, interesting to note that the psychological mechanisms, set going initially by psychological factors, were still at work in the final stages, colouring the contents of the mental state. This points to the importance of analysing in each case how far the symptoms can be explained on the psychological level, how far it is necessary to refer them to physical mechanisms. Of the latter the endocrine influence on mental function is one important aspect which needs much further investigation.

The endocrinologist, in his observations, has been concerned chiefly with the physical, organic consequences of endocrine upset, while the concomitant mental state, so necessary for further psychiatric understanding, is sometimes barely described, but the psychobiological approach is of practical importance and in the severer forms of humoral upset, such as Cushing's syndrome, its adoption would certainly lead to the eliciting of mental symptoms of greater or lesser degree and to increased knowledge of the factors responsible for the various syndromes.

We wish to thank Professor E. Mapother and Dr. Wooton for permission to use the clinical data ; Mr. Cairns for the operation notes ; and Professor Golla and the staff of the Central Pathological Laboratory for some of the pathological investigations.

Notes on Pathological Examination

Summary of Macroscopic and Microscopic Findings.—Sero-fibrinous pleurisy (10 oz.) of left sac. Clear effusion (about 6 oz.) in right pleural sac. Fibrous adhesions uniting upper lobe of left lung to parietal pleura over fourth and fifth ribs. Chronic bronchiectasis and purulent broncho-pneumonic consolidation of lower lobe of left lung. Purulent broncho-pneumonia of upper lobe of right lung. Œdema and congestion of remainder of lungs. Fatty degeneration of myocardium. Slight tortuosity of coronary arteries. Slight general atheroma. Back-pressure atrophy of centres of lobules and slight fatty degeneration of liver. Slight congestion of spleen. Mucous catarrh of stomach. Areas (up to 16 cm. long) of discrete and confluent recent hæmorrhage and necrosis in mucosa of lower jejunum and upper ileum. Chronic Bright's disease (nephritis repens, type IV). Small ovaries containing microscopically a few corpora fibrosa and one Graafian follicle. Infantile uterus (cervix, 3·5 cm. long ; body, 3·0 cm. long). Uniform hyperplasia of cortex of supra-

renal bodies. Normal colloidal thyroid gland. Four normal parathyroid glands. Cyst (0·7 cm. diam.) in head of otherwise normal pancreas. Glandular tissue in excess of adipose in thymus. Small pituitary gland in intact sella turcica showing perforation (0·05 cm. diam.) in its right lateral border corresponding to site of radon seed. No radon seeds found. Atrophy of right optic nerve, showing operative division immediately anterior to chiasma. Slight atrophy of frontoparietal convolutions. Healed fractures in costal ends of all right ribs and in lower left ribs. Osteoporosis (macroscopic) of ribs. Bodies of lumbar vertebræ easily cut with cartilage knife. No macroscopic evidence of osteoporosis in corticalis of femur. Petechiæ in skin of thorax. Faint diffuse brown pigmentation of skin of neck and less marked of face. Bruising of skin over anterior borders of both tibiæ. No striæ albicantes present. Excessive growth of hair in moustache and beard areas and over sides of cheeks. A greatly wasted woman with no local adiposity.

Pituitary gland, 0·4 gm.; suprarenal bodies, 24·45 gm.; ovaries, 7·4 gm.; thyroid, 17·3 gm.; thymus, 11·05 gm.; parathyroid glands, 130 mg.; heart, 276 gm.; kidneys, 248 gm.; pancreas, 55·5 gm.

The pituitary gland was divided horizontally and both halves were embedded together in paraffin. Serial sections stained with a modification of Mallory's acid-fuchsin anilin-blue method (Crooke and Russell (1935)) show no adenoma. Around gaps where the radon seeds had been inserted in the anterior and right lateral borders of the anterior lobe there are broad zones where the cells have been completely destroyed, leaving an acellular collagenous stroma (Fig. 3). In the remainder of the anterior lobe there is a remarkable diminution in the number of basophil cells, most of which show the peculiar hyaline change described by Crooke (1935). The acidophil cells are abundant and their granules well preserved. The remainder of the gland appears normal. Sections in the coronal plane through the anterior part of the right and left hypothalamus show an area (0·4 × 0·3 cm.) of complete necrosis in the optic chiasm, immediately to the right of the middle line. It extends ventrally to the pia and dorsally to the subependymal glia of the floor of the third ventricle. Surrounding this area is a fringe of compound granular corpuscles, and these are also sparsely scattered throughout the remainder of the chiasm. There is diffuse gliosis throughout the chiasm and many of the myelinated fibres have been destroyed except at the left border. The left supraoptic nucleus is well preserved, but many neurones have disappeared from the right.

Comment

This case is clearly an example of Cushing's syndrome. All the characteristic clinical features were present at some period of the illness, except cutaneous striæ, the absence of which suggests that the abdominal obesity was never great. Transient obesity was, however, noted in Case 1 of the report by Russell, Evans, and Crooke (1934), in which Cushing's syndrome was associated with a basophil adenoma of the pituitary in a male subject.

Pathological examination revealed no tumour in any of the endocrine glands. Several examples of the syndrome are, however, on record in which a similar negative result was obtained: Rutishauser (1933), Case 3; Kepler et al. (1934), Case 1; de Jongh (1935); Ulrich, quoted by Rasmussen (1936). Diffuse

hypertrophy of the suprarenal cortex and atrophy of the sex organs were however, present, and have been recorded in similar cases. Further the hyaline change in the cytoplasm of the basophil cells in the pituitary gland was well marked, and this in our experience is so conspicuous and constant a finding in other examples of Cushing's syndrome that it may be regarded as a diagnostic feature. The great paucity of basophil cells in the pituitary is difficult to explain. Without confirmatory evidence it can hardly be attributed to a specific selective effect of the radon. On the other hand, it has been observed (Crooke, 1935) that the number of basophil cells in the acini of the anterior lobe varies greatly in different examples of the syndrome. In Case 2 of his series it was noted that the reduction in the number of basophil cells was so great that the sections were comparable in this respect to the pituitary gland in Addison's disease. It is likely, therefore, that the extreme reduction in the present case is independent of the insertion of radon seeds.

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Fig. 2.—Patient after onset of Cushing's Syndrome.

Fig. 1.—Patient before onset of Cushing's Syndrome.

Fig. 3.—Horizontal section of pituitary gland showing areas of destruction by radon seeds. Mallory's acid-fuchsin anilin-blue ; ×6·5.

A CRITICAL REVIEW

PRIMARY DISEASES OF VOLUNTARY MUSCLES

BY

S. NEVIN

From King's College Hospital and Maida Vale Hospital for Nervous Disease, London

Introduction

THE voluntary muscular system forms in an average male about 43 per cent. of the total body weight. It is a very uniform system and is composed of aggregations of individual muscle fibres each of which are complex multinucleated cells, consisting of a sarcolemmal sheath and its nuclei, a motor end plate, and contractile substance. This system is affected by a large group of primary diseases, i.e. diseases in which the essential disturbance of function is most probably located in the muscle fibre or myoneural junction. The pathogenesis of all these diseases, which have been clearly recognized clinically for half a century, has so far remained obscure. In recent years, however, advances in the physiology of the muscle fibre, especially as regards the chemistry of muscular contraction and the transmission of normal excitation from nerve to muscle, have opened up new methods of approach to the study of muscular diseases and much work along these lines has already been done. The results so far are perhaps infinitesimal compared with the vastness of the problems awaiting solution, but it is to be hoped that they are only the first fruits of greater advances in the immediate future. The time now appears opportune to survey the work in this field, to evaluate the studies which have so far been published, and to discuss the lines along which further progress is likely to be made. It would not be possible in the compass of a short review to deal in detail with all aspects of primary diseases of voluntary muscle. Attention must therefore be specially directed to the results of recent biochemical studies and only such clinical, therapeutic, or histological details included as are necessary to make the review comprehensible.

It will also be necessary to exclude from consideration the large group of inflammatory diseases included under the term " myositis " and also such muscular abnormalities as cramp, myokimia, and the weakness in Addison's disease.

Progressive Muscular Dystrophy

Muscular dystrophy or myopathic atrophy is a disease in which large groups of voluntary muscles undergo primary degeneration. The age of onset

and the location of the affected muscles have led to the recognition of several clinical types of the disease, but as far as is known at present there is no essential pathological difference between these types. The histological features of the affected muscles have so far given no clue to the cause of the disease, but little attention has been paid to the anatomical changes since their first description. This is to be regretted, because it is clear that there is much to be learned about the appearance of the muscle fibre in the premyopathic stage, the sequence of changes in a degenerating fibre, and the variation of the histological picture with the rapidity of the degeneration. It is also possible that with the development of histochemical methods information may eventually be gained about the chemical process accompanying the degeneration. As far as one can see at present, however, this degeneration would appear to be secondary to alterations in the actual protoplasm of the fibre, about the nature of which we have no idea. The problem appears very difficult, but neither this difficulty nor the fact that the disease is hereditary and familial precludes the possibility that it might be possible to alter the course of the disease were the biochemical changes associated with the muscle degeneration discovered. For this reason the recent biochemical researches in this disease and the methods of treatment founded thereon have been followed with great interest. These researches have centred round the role of creatine in the metabolism of voluntary muscle and the discovery that the amino-acid glycine is a precursor of creatine in the human body.

Creatine-Creatinine Metabolism and the Changes produced by Glycine

It will be necessary right at the outset to call to mind some simple facts and chemical relationships with regard to creatine and muscle physiology. Creatine is a chemical constituent of striated muscle and 98 per cent. of the creatine in the body is to be found in this tissue. In muscle it is linked up with phosphoric acid in a highly labile compound usually termed phosphagen. The breakdown of this compound and its resynthesis play an important part in the chemistry of muscular contraction, which also involves other important reactions, namely the breakdown of glycogen to lactic acid through certain soluble carbohydrate esters and the breakdown of adenosine triphosphoric acid (adenyl pyrophosphate). The full details and significance of these changes are not fully understood. As a result of the endogenous muscle metabolism creatinine, which is the anhydride of creatine, is excreted in the urine to the extent of about 23 mg. per kilogram of the body weight in the 24 hours. This is the creatinine coefficient, and it is a fairly constant figure for each individual and is directly related to the total mass of voluntary muscle.

In the adult male no creatine is excreted in the urine, because it is all metabolized or stored in the muscles ; but in children up to seven years of age and periodically in some adult women some creatine is excreted in the urine. Although the origin of creatine in the body is not definitely known, this can only mean that in children more creatine is formed in the body than can be metabolized by the muscles at this stage in their development. The reason for the periodic excretion in women is not known.

In such conditions as diabetes, exophthalmic goitre, and during periods of fever and starvation creatine appears in the urine, so that increase in endogenous metabolism of muscle from different causes prevents the storage and conversion into creatinine of the normal amounts of creatine. This will also happen if a large amount of muscle tissue is lost, as through the amputation of a limb.

From these observations it is to be expected that in cases of muscular dystrophy where there is considerable loss of muscle tissue with impairment of function of the remainder, alteration would occur in the normal output of creatinine in the urine. That such is the case has been known for a very long time.

Rosenthal (1870) reported the occurrence of decreased excretion of creatinine in cases of muscular dystrophy, and similar observations were made by others. Spriggs (1907–08) noted that the diminution of creatinine output was proportional to the extent of the muscular wasting. Levene and Kristeller (1909) first reported the excretion of creatine in the urine of patients with muscular dystrophy, and later workers confirmed this finding and the diminution of creatinine previously recorded, (McCrudden and Sargent, 1918 ; Janney *et al.*, 1918 ; and Bürger, 1919). So far, no special interpretation was placed on these findings, and they were in fact rightly regarded as indicating that creatinine was a product of muscle metabolism and that in advanced muscle diseases there was impairment in the conversion of creatine into creatinine, so that creatine as such was excreted in the urine and the creatinine output diminished. Brand *et al.* (1929), working from the physiological standpoint on the origin of creatine, found that the constant creatinuria of muscular dystrophy could be increased 40 per cent. by the administration of the amino-acid glycine. This observation was confirmed by Thomas *et al.* (1932) and Milhorat *et al.* (1932), who found, however, that if the administration of glycine were prolonged for a period of 2–8 weeks, there resulted a considerable clinical improvement in the patients. In the last four years numerous workers have concerned themselves with the biochemical and therapeutic effects of glycine in muscular dystrophy. This work has resulted in the repeated confirmation of the changes in the creatine-creatinine excretion and the effect of glycine on the creatinuria in this disease. It has also been repeatedly shown that a lowering of the creatine tolerance also takes place. Normally in an adult if 1 gm. of creatine is administered by the mouth it is entirely stored in the muscles, and none appears in the urine. In muscular dystrophy, however, a large percentage of the ingested creatine may be excreted within 24–48 hours, and the greater the loss of muscle tissue the greater will be the lowering of the creatine tolerance. The reports in respect of the therapeutic effects of glycine are, however, very divergent, considerable improvement being reported by some (Kostakow and Slauck, 1933 ; Tripoli and Beard, 1934 ; Cuthbertson and Maclachlan, 1934) and no improvement by others (Brand and Harris, 1933 ; Mettel and Slocum, 1933 ; Börst and Moebius, 1936 ; and Bargi, 1937). Milhorat (1933) and Reinhold *et al.* (1934) have reported histological changes in dystrophic muscle following glycin therapy, which they considered indicative of improvement in the disease. These changes consisted in greater uniformity in fibre size, better staining reactions,

decreased numbers of visible nuclei, and decreased fat content of the muscle. Bargi (1937) has, however, not been able to confirm these findings.

It is somewhat difficult to understand why so many papers have been published on this subject, unless it has been due to the possibility that the supposed beneficial effects of glycine administration corrected some underlying biochemical abnormality of the disease. It was not long after the publication by Thomas *et al.* (1932) of their findings that other workers suggested this possibility. Thus Kostakow and Slauck (1933) in their paper suggested that the underlying disturbance in muscular dystrophy might be the inability of the muscles to absorb and utilize creatine, and that this was corrected by glycine. Tripoli and Beard (1934) even wrote that in this condition after glycine treatment the creatine retained as creatine phosphoric acid in the muscles served over and over again to supply the energy for muscular contraction and the muscular efficiency increased at a remarkable rate. Also, more recently, Braestrup (1936) has stated that the facts with regard to the metabolic changes in muscular dystrophy indicate that the function of decomposition and recomposition of creatine phosphoric acid is radically impaired in this disease.

Unfortunately there is little justification for any of these statements, and it would seem that they could only have been suggested without due regard to all aspects of the question, and neglect of the obvious methods open for their confirmation or rejection.

In the first place the increased excretion of creatine following the administration of glycine does not necessarily suggest a fundamental defect in the creatine metabolism of the muscle, because, as is well known, the blood creatine in muscular dystrophy is normal and there is no evidence of any deficiency of creatine for the needs of the muscle. From the known physiology of creatine and creatinine already briefly stated it will be clear that criterion of an improvement of function in the muscles would have been a very definite increased excretion of creatinine, but such does not occur. Seeing that the increase is entirely in the creatine, this can only mean that glycine is a precursor of creatine and leads to the increased formation of creatine in the body, which is excreted and not stored owing to the widespread disease of the muscles, so that the administration of glycine is nothing more than an indirect creatine tolerance test. Thomas and his co-workers (1932) have stated that after prolonged administration of glycine the creatinine content of the urine does rise to some extent and the creatine content falls. These changes are, however, slight and are probably only expressive of general metabolic changes in the body following the administration of large doses of glycine. It is possible that the more normal muscles may come to metabolize slightly more creatine and that less creatine may be formed for some time after the discontinuance of an important precursor in the pure state. Apart from these considerations, the matter is put beyond dispute by the fact that in cases of extensive secondary wasting of muscles following disease of the nervous system, such as progressive muscular atrophy, similar changes in the creatine-creatinine excretion may be found and an increase of creatine output after the administration of glycine. This fact has been known since the intensive studies of creatine-creatinine metabolism in

muscular dystrophy began, but has been simply disregarded. Milhorat and Wolff (1937) in a recent paper confirm this fact and promise in a further paper details of the changes in cases of secondary muscle atrophy. It is only to be expected that in such cases the extent of the metabolic changes will be less, this being simply due to the more localized nature of the muscle disease in such conditions, as compared with muscular dystrophy, where practically the whole voluntary musculature may be wasted or abnormal. These observations also rule out the possibility of the effect of glycine on the creatine excretion being used as a method of differential diagnosis. It is not, however, to be denied that some information may be gained from its use, and also from the creatine tolerance, because in cases of muscular disease with only slight creatinuria a marked increase after glycine or the administration of creatine may occur and indicate a more widespread affection of the muscles and a greater inability to store creatine than was likely from the degree of spontaneous creatinuria or the degree of muscle-wasting. Milhorat and Wolff (1937) have reported the occurrence of the same degree of spontaneous creatinuria in a case of muscular dystrophy and myasthenia gravis, but in the latter the creatine tolerance was much higher, and the creatinuria following glycine less than in the case of muscular dystrophy. Such tests are, however, of little clinical value and would not repay the laborious chemical investigations necessary.

Direct Investigation of the Muscle Chemistry in Muscular Dystrophy

This brings us to the consideration of possible abnormalities in the important chemical compounds in muscle whose interreactions subserve muscular contraction. Observations have been made on the creatine phosphoric acid, the adenosine triphosphoric acid, the glycogen, lactic acid, and soluble carbohydrate, and the esters in dystrophic muscle removed at biopsy.

In an investigation of the phosphorus-holding compounds in muscle from patients with primary muscular degeneration, Nevin (1934 and 1936) found that there was present a considerable diminution of the total acid-soluble phosphorus expressed as milligrammes per gramme of wet muscle. This varied from case to case, and was considered most likely due to the varying fat and fibrous tissue increase in the muscle specimens. An individual examination of the various compounds making up this total showed some slight differences from the normal in the percentage of the total acid-soluble phosphorus of each compound. These differences consisted in a lowering of the creatine phosphoric acid and an increase in the soluble carbohydrate esters, but with no change in the adenosine triphosphoric acid. Debré *et al.* (1936) have also reported considerable diminution of the total acid-soluble phosphorus in the muscle from three patients, with a lowering of the total phosphagen and adenylpyrophosphate expressed as milligrammes P_2O_5 per gramme of wet muscle. The percentage of phosphagen of the total acid-soluble phosphorus was approximately normal in two cases, but lowered in the third, and the percentage of adenylpyrophosphate was lowered in all three. They apparently did not consider the lowering of the total acid-soluble phosphate as entirely due to the

increase of fat and fibrous tissue in the muscle, and they found the lactic acid and glycogen content of the muscles normal. Collazo *et al.* (1936) reported diminution of total acid-soluble phosphorus (expressed as milligrammes per 100 grammes of wet muscle), inorganic phosphate, phosphagen, and glycogen in the affected muscles in six patients with muscular dystrophy. The figures for lactic acid, on the other hand, approximated closely to normal and the percentage of phosphagen in the total acid-soluble phosphorus was also normal.

In the first place it will be clear that these observations lend no support to the theories which suggested that because glycine produced creatinuria a fundamental abnormality in the creatine phosphoric acid metabolism in the muscle existed. Such does not exist, and in one case showing a considerable creatinuria following glycine, Nevin (1936) found that the percentage of creatine phosphoric acid of the total acid-soluble phosphorus was normal.

The question remains, however, as to the significance of the alterations from the normal which have been recorded. Clearly the increase of fat and fibrous tissue must account in greater or less degree for the general diminution of the chemical compounds. This is borne out by the great variation in the analysis in different cases, probably related to the degree of atrophy in the muscle examined. The possibility of some diminution of the compounds in the actual muscle fibre is not excluded, and the increase of fat and fibrous tissue will not account for the lowered percentage of creatine phosphoric acid of the total acid-soluble phosphorus. This, however, has not been present in all the analyses reported, and it has been shown (Nevin, 1934) that creatine phosphoric acid breaks down during contraction of dystrophic muscle and is reformed during rest to an extent only slightly less than normal. A similar alteration in creatine phosphoric acid has been found in muscle undergoing atrophy secondary to nerve degeneration, so that it would appear that these changes are in some way secondary to the degeneration of the muscle in muscular dystrophy, and that they do not indicate specific chemical alterations in this disease.

Elkington and Goldblatt (1933) have found a diminished response in the rise in blood lactate on injection of adrenaline and no definite alteration in the hypoglycæmia in three myopathic patients. The resting values for lactate and glucose were within normal limits. These observations would correspond with the finding of a lowered glycogen content in the muscles by Collazo *et al.* (1936), because the lactic acid is derived from the muscle glycogen, but there is nothing to indicate that the changes from the normal are not due to the general diminution of muscle in which glycogen can be stored.

While concluding that so far the biochemical investigations, direct and indirect, in cases of muscular dystrophy have afforded results which can only be regarded as secondary to the muscle degeneration, it is clear that the question of the significance of abnormalities in the chemical compounds of dystrophic muscle cannot be considered closed. Further investigations of the chemistry of the living muscle removed at biopsy is clearly a fruitful line of research, and it may be that with advances in the normal chemistry of muscle, the introduction

of new methods may reveal for us at least the biochemical paths along which degeneration is taking place.

Therapeutic Effects of Glycine

Having found in the biochemical relationship involved no rational basis for the use of glycine as a therapeutic agent in muscular dystrophy, it remains to discuss the possible beneficial effects and their explanation. That the beneficial effects must be slight in degree and confined to special cases, such as those without advanced muscular wasting, follows from the numerous negative findings that have been reported. On the other hand, it can hardly be doubted that some improvement is experienced in suitable patients. Armstrong and Herbert (1935) have published their earlier results, and in a recent personal communication Armstrong states that advanced cases, especially of the pseudo-hypertrophic variety, do not benefit but become progressively worse, whereas those classified as Erb's Juvenile variety, and presumably less extensive and progressing less rapidly, do generally show improvement only while the administration of glycine is maintained. He has, however, noted that some patients seem to progress with extreme rapidity after the glycine is stopped, and in one such case he found the histological changes more intense than those present in a biopsy before the administration of glycine.

There can be no question of any specific effect of glycine in cases of muscular dystrophy, and there does not seem to be any explanation for the beneficial effects in some cases, other than that the specific dynamic effects of large doses of glycine leads to stimulation of metabolism in the muscles. This may act more through the healthy muscle fibres that remain than the actual degenerating fibres. The question as to whether this treatment may not be harmful in some cases has also to be considered, and it is doubtful if it should be used in other than selected patients who are still able to get about and take at least some active part in life. Here the increased feeling of well-being and slight general improvement may be important. Possibly small doses continued over monthly periods, with weekly free intervals and larger doses on special occasions, as advised by H. (1936), is the best way to use glycine in muscular dystrophy.

Further Theories and Methods of Treatment in Muscular Dystrophy

Kuré (1927) claims to have shown that voluntary muscle receives both a sympathetic and a parasympathetic nerve supply from the posterior roots, and that lesion of both these nerve pathways produces dystrophic changes in the muscles. On the basis that progressive muscular dystrophy is a disturbance of the autonomic innervation of voluntary muscle, Kuré (1930) has recommended treatment with injections of adrenaline and pilocarpine. He gives 0·2 c.c. of a 1 per cent. solution of pilocarpine and 0·2 c.c. of a 0·1 per cent. solution of adrenaline daily or every other day for 50 doses, and claims to have produced improvement in his patients and prevention of the progress of the disease. There is no scientific basis whatever for this theory, and it is not surprising that most reports record no beneficial results from the treatment

(Reese *et al.*, 1935 ; Paulian, 1934 ; and Curschmann, 1933). Hough (1933), on the other hand, reports benefit, but states that progression may occur while under treatment. This latter observation excludes the possibility of any specific effect from the remedies, and the benefit found was probably in large part psychological, as the author himself suggests.

Hirata and Suzuki (1937) have reported that in cases of muscular dystrophy they found a diminution of the output of vitamin C in the urine and also less of this substance in the cerebrospinal fluid. An analysis of diseased muscle showed a diminution in glycogen and creatine phosphoric acid, and it is claimed that the administration of vitamin C corrected those abnormalities and led to remarkable clinical improvement. The author's figures show a clear increase in the percentage of phosphagen in relation to the total acid soluble phosphorus after treatment. There are, however, no figures from control experiments, and the figures for the total acid-soluble phosphorus are so much higher than those recorded by other workers in normal muscle that it is very difficult to assess the value of his results. Also, it would appear unlikely that vitamin C deficiency could occur in such a manner as to cause only symptoms referable to the muscles.

In the recent Italian literature Meldolesi (1936) and Bompiani and Meldolesi (1936) have described defective proteolytic function of the pancreas in cases of muscular dystrophy. They have associated this with slight anatomical changes in the pancreas, and they record improvement in their patients by treatment with pancreatic extract. Barasciutti (1937) has, however, been unable to confirm these findings, so that the changes recorded were probably unrelated to the muscular dystrophy.

In concluding this section on muscular dystrophy it has to be observed that the biochemical researches of the last few years have led to little real advance in the knowledge of the disease. The alterations from the normal which have been recorded are entirely secondary or indirect effects of a pathological process the essential nature of which is still obscure. A great expenditure of time and energy has been wasted in repeatedly confirming these indirect results, to the consequent neglect of more fruitful lines of research. These clearly are to hand in histochemical and direct chemical investigation of degenerating muscle. Along these lines the paths of the muscle degeneration may be worked out, and it is not impossible that more beneficial methods of treatment may be evolved.

Myotonia and the Diseases in which it occurs

Myotonia is a clinical condition characterized by delay in relaxation of voluntary muscle after natural, mechanical, or electrical stimuli. It is found predominantly in two diseases, dystrophia myotonica and myotonia congenita, but in the latter the myotonia is generally more marked and more widespread.

It has been known for many years that both electrical and mechanical myotonia can occur in myotonic muscles following blocking of the motor nerve. This naturally led to the view that the essential functional abnormality

in the phenomenon was peripherally situated. Gregor and Schilder (1913) and Bürger and Schellong (1923) found that myotonia was associated with action currents. With the less sensitive methods of examination then available it was not always possible to demonstrate the occurrence of such action currents, but in recent years this observation has been confirmed by Delmas-Marsalet and Bargue (1934) and Lindsley and Curnen (1936).

The association of characteristic action currents with the delayed relaxation in myotonia indicates clearly that the phenomenon is in some way an abnormality of excitation of the muscle fibres, and there is furthermore no evidence that it could be purely myogenic in origin.

Lindsley and Curnen (1936) consider that myotonia is reflex in origin, and is due to the persistent discharge of hyperexcitable sensory end organs in the muscle. These workers leave out of consideration entirely the occurrence of myotonia after block of the motor nerve, so that while it is impossible to say that reflex action may not play some part in the production of myotonia under natural conditions, it is obviously no explanation of the phenomenon. Clearly some abnormality at the neuromuscular junction must be present.

Recent observations on the effects of drugs in myotonia lend support to this view. Lanari (1936) has found that, while the intra-arterial injection of 0·04 gm. of acetylcholine produced no motor effect in normal subjects, in patients with myotonia it gives rise to a painful reversible muscular contracture lasting about 30 seconds. This does not occur if the acetylcholine is injected into the muscle directly. There is now clear physiological evidence that acetylcholine plays some part in the transmission of the motor impulses from nerve to voluntary muscle (Dale *et al.*, 1936), so it is legitimate to conclude that the abnormal action of the intra-arterial injection of acetylcholine in myotonia is produced at the neuromuscular junction. Furthermore, Russell and Stedman (1936) have found that myotonia can be increased by the administration of prostigmin and large doses of potassium chloride or potassium citrate, and both prostigmin and the potassium ion are known to potentiate acetylcholine transmission at nerve junctions. Russell and Stedman suggest that myotonia may be due to an excessive production or accumulation of acetylcholine at the motor nerve-endings. They also found that ethyl alcohol temporarily relieves myotonia, and Kennedy and Wolff (1937) have found that quinine hydrochloride has a similar effect. There is no evidence to show that ethyl alcohol and quinine act at the neuromuscular junction, but their effect is most likely to be produced at this site.

It seems most probable, therefore, that myotonia is produced by some abnormality at the neuromuscular junction, but as regards the cause and nature of this abnormality nothing is as yet known. It may be primarily dependent upon a hyperexcitability of the nerve ending to the chemical transmitter, or it may be due to excessive accumulation of acetylcholine at some stage of contraction and relaxation, with which may be associated an abnormal esterase function. The clinical and physiological facts available do not permit of any definite statement. It is also probable that the full development of myotonia clinically is dependent upon the way the muscle is innervated. If a muscle is

directly innervated it may be absent and yet appear when the muscle is contracted to a similar extent synergically.

It has also been observed clinically that the myotonia following the movement of grasping is in reality an addition of contraction in some muscles rather than a delay in relaxation. Future investigation must therefore be directed to the nature of the peripheral abnormality and the nature of the central innervation which combines with it to produce voluntary myotonia.

Diseases in which Myotonia occurs

In dystrophia myotonica the predominant features of the disease are the muscular dystrophy and the general endocrine changes. No definite relationship has been established between these changes, and their relation to the myotonia is also unknown. It might seem likely that the dystrophic changes in the muscles led to abnormalities in the nerve-endings which gave rise to the myotonia, but Devry and Everard (1936) have described members of families in which myotonia was present without muscular atrophy or endocrine changes. On this account it would seem probable that the myotonia was not secondary to the muscular atrophy or the endocrine changes. The muscular aspect of dystrophia myotonica consists, therefore, in a primary degeneration of the muscle fibre and an abnormality at the neuromuscular junction, resulting in delayed relaxation. This is in contrast to myotonia congenita, where there are probably no primary changes in the muscle fibre and the neuromuscular abnormality constitutes the disease. The only constant histological change in the muscles in the latter disease is the hypertrophy of the individual fibres. This is most probably secondary to the myotonia, because if during voluntary movement each contraction is followed not by relaxation but by a varying degree of additional contraction, hypertrophy of the muscle fibres might be expected to result.

It is interesting to compare the creatine-creatinine metabolism in dystrophia myotonica and myotonia congenita. In the former the changes are similar to those found in muscular dystrophy, but in the latter no creatine is excreted in the urine, there is an increased creatine tolerance, and the creatinine content of the urine is a high normal. These findings in myotonia congenita are exactly what one would expect to occur, because the muscular hypertrophy leads to greater ability to store creatine and convert it into creatinine, the natural end-product of muscular metabolism. Poncher and Woodward (1936), who have reported the increased creatine tolerance in myotonia congenita, state that in a patient with this disease they found that creatine administration accentuated the myotonia. It is difficult to suggest an explanation of this observation on the basis that the myotonia is primarily an abnormality situated at the myoneural junction, but it is equally difficult to explain it as a direct effect on the contractile substance of the muscle fibre. In this connection reference must be made to another case described by Poncher and Woodward (1936). This was a male infant of 5 months in which there was present marked hypertrophy of all the muscles of the body. The muscles showed a localized

dimpling and sustained contraction on percussion. The child was subject to generalized muscular spasms which were regarded as myotonic in nature. There was an absence of the physiological creatinuria of infancy and childhood. Creatinuria was produced by the administration of thyroid extract, and at the same time the myotonia and muscular hypertrophy disappeared. Myotonia could, however, be produced by the ingestion of creatine. The authors took the view that the patient was not suffering from hypothyroidism and that the case was one of myotonia congenita, in which the symptoms were relieved by thyroid medication. They suggest that some abnormality in the intrinsic chemical mechanism of muscular contraction may account for the abnormal metabolism of creatine in this case of myotonia congenita, and that the beneficial effects of thyroid may result from alterations in this abnormal metabolism. It is admitted, however, that no explanation is available as to why adults with myotonia congenita are not benefited by thyroid extract. The case cannot, however, be easily accepted as a case of myotonia congenita. The age of onset of the symptoms, the enlargement of the tongue, the lack of spontaneous movements, and the atypical nature of the myotonia all suggest strongly that thyroid deficiency was present in the patient, and that the case really falls into the group of muscular hypertrophy and myotonia associated with hypothyroidism. The authors, however, reject this explanation of the case. There are no analyses recording changes in the muscle chemistry in myotonia congenita, and this case cannot be taken as evidence that such are likely to be found. Morgulis and Young (1931) have also suggested that in dystrophia myotonia there is a failure of the muscle to synthesize phosphagen. There is no evidence for this statement, and the chemical changes in the muscle in this disease are similar to those in progressive muscular dystrophy. It cannot, therefore, be accepted that abnormalities in the intrinsic chemical mechanism of muscular contraction are of primary importance in myotonia congenita or dystrophia myotonica.

Muscular Hypertrophy and Myotonic-like Symptoms associated with Hypothyroidism

In recent years several cases exhibiting these features have been described in the literature. Weitz (1931) described a 44-year-old man who developed myxœdema after operative treatment for exophthalmic goitre. In this patient the muscular system throughout showed increased tonus and sudden movements led to painful cramp in the muscles, which became very hard and boardlike. Percussion of the muscles caused localized contractions which lasted some seconds and slowly relaxed. Movements became quicker on repetition. Electrical hyperexcitability of the nerves and muscles was also present. The author considered the symptoms as closely related to myotonia and secondary to the myxœdema. He refers to descriptions in the older literature of spastic muscles and myotonic reactions in myxœdematous patients. Garcin *et al.* (1935) have reported in great detail the occurrence of Thomsen's syndrome in association with myxœdema in a young man of 28. In this case the myotonic disturbances

of voluntary movement were associated with hypertrophy of the muscles. Bourguignon and Garcin (1935) noted that the myotonia was of shorter duration than occurs in Thomsen's disease. Histologically there was found a variable hypertrophy of the muscle fibres which might not involve the whole length of the fibre. There was some increase of interstitial tissue, and in places accumulations of histiocytes between the muscle fibres. The authors consider that possibly both the myotonia and myxœdema were secondary to some central nervous disturbance. Debré and Sémelaigne (1935) and Eckerström (1936) have described patients with somewhat similar features, the former in infants and the latter in an adult. In Garcin's case no record is given of the effect of thyroid medication, but in the others this led to a disappearance of symptoms, which shows clearly that the condition is quite distinct from myotonia congenita. It is probable, therefore, that careful clinical and electrical analyses of the myotonic-like reactions in the muscles will show that these are essentially different from true myotonia. It is clear, however, that in some patients hypothyroidism may be associated with hypertrophy and myotonic-like symptoms affecting the voluntary muscles. The muscular symptoms are directly related to the hypothyroidism, and it is very difficult to suggest an adequate explanation for their occurrence. It does not appear very probable that changes in the muscle chemistry can be the primary cause, because it is difficult to see how slowness of relaxation from this cause could lead to the muscle hypertrophy. Some abnormality of excitation would seem necessary to account for the very great tension which develops in the muscles after contraction. It is possible that in these cases some chemical abnormality is present at the myoneural junction which linked up thyroid deficiency can give rise to the myotonic-like symptoms and muscular hypertrophy. In Poncher and Woodward's (1936) case, which was considered to belong to this group, the administration of creatine produced myotonia at a time when the patient was free from symptoms. This observation may hold a clue to the underlying chemical changes which produce the abnormal muscular reactions.

Myotonia Acquisita

Myotonia acquisita is a condition very similar to myotonia congenita, but differing from it in not being congenital or hereditary, and developing later in life, after infection or trauma or without recognizable cause. Krabbe (1934) considers that true muscular hypertrophy and myotonia acquisita are variations of the same abnormality, namely, an abnormal regeneration after neuritic processes, and that hypertrophy of the muscle sarcoplasm results in the myotonic condition. Cases of this nature are rare, and consequently there are no reports of the effects in this condition of drugs known to influence the myotonia in Thomsen's disease. The myotonia in the two conditions is, however, very similar clinically, and it is possible that also in myotonia acquisita some abnormality at the neuromuscular junction constitutes the major pathology of the disease. If the myotonia in myotonia acquisita were primarily dependent on an abnormality of the sarcoplasm it must be considered quite distinct from

that associated with Thomsen's disease. The cases of muscular hypertrophy without myotonia which Krabbe considers related to myotonia acquisita may possibly be examples of muscular dystrophy in which a preatrophic stage of generalized muscular hypertrophy is a very prominent feature.

Myasthenia Gravis

Myasthenia gravis is a disease characterized by weakness and rapid fatiguability of the voluntary muscles. The clinical features of the disease have been known for over half a century, but the nature and site of the loss of function have always presented most baffling problems to the clinical investigator. It is, however, clear from the spontaneous remissions, in some cases approaching practically complete recovery, that a remediable cause underlies the pathology of the condition. The anatomical changes in the disease have been fully investigated with the following results. Slight changes have been found in the nervous system in some cases, but these have never been accepted as being causally related to the disease. The affected muscles show no abnormality except the presence of lymphorrhages, which consist of small collections of lymphocytic cells between the muscle fibres. Such collections of cells are also found in other organs as well as in the muscles. Hyperplasia, or a tumour of the thymus gland, is the only other abnormality reported. The significance of this finding has been disputed because it is not constantly present, but in reference to this point Greenfield (1923) stated that unless the mediastinum was carefully searched the presence of abnormal thymus tissue might be easily overlooked.

The biochemical investigations in the disease have so far yielded negative results. The earlier studies were conflicting and they will not be described as details are to be found in an article by Keschner and Strauss (1927). Marburg (1931) reported that he found the magnesium in the blood abnormally high (6 mg. per cent., the normal being 2–3 mg. per cent.) in a case of myasthenia gravis. He considered it possible that this increased concentration of the magnesium ion might be secondary to thymus hypertrophy and act by producing a curare-like action on the nerve endings of the voluntary muscle.

Boothby *et al.* (1932) have found, however, that the blood magnesium was normal in six cases and they also found no abnormality in the other inorganic or nitrogenous constituents of the blood. In this paper Edgeworth reported that in a detailed chemical examination of the urinary, blood, and fæcal constituents in her own personal case at a time when she was physically prostrate the only abnormality found was a slight creatinuria and lowered excretion of creatinine. A lowered creatinine excretion had already been reported by Spriggs (1907) and some degree of creatinuria with a low muscle content of creatine by Williams and Dyke (1922).

With the discovery of the effect of glycine on the creatine output in muscular dystrophy, Boothby (1932) studied the effects of glycine on myasthenia gravis, and reported clinical improvement possibly explained by the building up of the amount of creatine phosphoric acid in the muscles. In a fifth report Boothb

(1934) states that the fact that glycine decreases the fatiguability of the disease can no longer be questioned. Remen (1932) also found benefit from glycine in myasthenia gravis, and considered that this substance corrected abnormalities in the creatine-creatinine metabolism in the disease. It is definitely known that some degree of creatinuria which can be increased by glycine does occur in myasthenia gravis, but this affords no justification for the above assumption, as will be seen from the previous discussion in this review in relation to the creatinuria in muscular dystrophy. Furthermore, the chemical constituents of myasthenic muscle have been investigated and found normal both as regards the phosphorus-holding compounds at rest and on contraction (Nevin, 1934) and the glycogen and lactic acid content (Collazo *et al.*, 1936). Also Elkington and Goldblatt (1933) have found that the rise in blood lactate derived from the muscle glycogen after injection of adrenaline is normal. These findings also negative the suggestion by Costedoat and Aujeleu (1934) that the underlying fault in the disease may be the failure of the reconversion in the muscle of lactic acid into glycogen. This suggestion was based on the observation that in rabbits, muscles rendered poor in glycogen gave a myasthenic reaction. It follows from these observations that there is no definite evidence in myasthenia gravis of a primary chemical abnormality in inorganic or organic chemical constituents of blood, urine, or fæces ; nor in the intrinsic chemical mechanism of muscular contraction.

The beneficial effects of glycine have not been confirmed, and it is more than probable that it has no place in the treatment of myasthenia gravis. As repeated investigations failed to show any fundamental histological abnormality in the nervous or muscular systems or any biochemical alteration in the blood or muscle fibres, attention became directed to the myoneural junction as the probable site of the disturbance of function in the disease.

Holmes (1923) stated that the site of the lesion was peripherally situated and that disturbances of thymus function must play an important part in the pathogenesis of the disease. Support for this conception has been afforded by the discovery that two drugs, ephedrine and eserine, have a very beneficial effect on the disease and by experimental work on the relation of the thymus to muscular weakness.

The use of ephedrine was discovered by Edgeworth (1930), and although its effect is not so striking as that of eserine sulphate, it is more gradual and can be maintained over long periods, if no intolerance exists, by oral administration. The drug is very similar in its action to adrenaline, and McAlpine (1934) suggested that the explanation of its therapeutic effect might be related to the relief of fatigue in voluntary muscle which follows sympathetic stimulation. Corkell and Tiegs (1933) have shown that this effect is due to the transfusion of an adrenaline-like substance from the sympathetic nerve-endings to the neuromuscular junction. Injection of adrenaline has a similar effect, so it is very probable that ephedrine acts at the neuromuscular junction in myasthenia gravis, although the mechanism of its action is still obscure.

The beneficial effects of eserine sulphate in myasthenia gravis were first reported by Remen (1932). This worker, however, disregarded the observation

on account of the excessive vomiting produced by the drug and devoted his attention to studying the effects of glycine, as already described. Walker (1934) independently observed the effects of eserine in this disease, and by giving atropine controlled the unpleasant gastro-intestinal symptoms. She later reported that even better results could be produced with a related drug, prostigmin (1935), and since these observations the remarkable effect of these drugs in causing a recovery of function in the affected muscles has been repeatedly confirmed. Pritchard (1936) has also shown that it causes a return to normal in the form of the myasthenic myogram produced by high rates of stimulation. The effect is, however, entirely symptomatic, and leads to no maintained improvement in the patient's condition. In bulbar cases as the effect of the drug wears off aggravation of symptoms may occur. The introduction of oral administration (Everts, 1935), giving a more prolonged and gradual effect, seems to have increased the therapeutic value of prostigmin, but it would appear that its use must be guided by a careful study of the response of the individual patient. Apart altogether from its therapeutic value, there can be little doubt that its action is produced at the myoneural junction, thus indicating the site of abnormal function in the disease. It has been established that peripheral parasympathetic effects are transmitted by the liberation of acetylcholine, which is rendered inactive by an enzyme in the blood and tissues called choline esterase. The activity of this esterase is inhibited by prostigmin and analogous drugs. As already stated, Dale (1936) has furnished evidence that acetylcholine is also liberated at the myoneural junction in voluntary muscle during excitation, and the remarkable effect of prostigmin can therefore be explained by supposing that its action in delaying the destruction of acetylcholine corrects some abnormality of neuromuscular transmission at this point. The nature of this abnormality is still entirely obscure.

An attempt has been made to gain some information thereon by estimating the choline esterase in the serum. Stedman and Russell (1937) have found that the average content of the esterase in the serum is lower than normal. Pilcher (1937) in seven cases also reports a similar finding. McGeorge (1937) has considered, however, that in his three cases the esterase content fell within normal limits. Even if it be accepted that a slight lowering of the serum esterase is present in myasthenia gravis, its significance is difficult to assess because the relation of the serum esterase to that in the tissues is not known. It might be taken to indicate a tendency for the esterase in the muscles to be low and this again might indicate a diminution of acetylcholine activity, as the amount of esterase in a tissue and its acetylcholine activity are roughly parallel. The low value for serum esterase seems, however, to exclude excessive destruction of acetylcholine as the abnormality at the myoneural junction.

It is possible that this abnormality consists in defective formation or mobilization of the chemical transmitter. Fraser *et el.* (1927) interpret the beneficial effects which they have observed in myasthenia gravis following the subcutaneous injection of acetylcholine, carbaminoylcholine and acetylbeta-methylcholine as most likely indicating a defect of this nature. Briscoe (1936)

has, however, shown that mild curarization experimentally can produce a myogram very similar to that found in myasthenia gravis with a fast rate of stimulation, and which similarly returns to normal with prostigmin. Now curarization does not affect the liberation of acetylcholine (Dale *et al.*, 1936) so it would seem more probable that the threshold of excitation was in some way abnormally raised. This is not likely to be due to any anatomical change at the neuromuscular junction, as the variability of the condition and the absence of muscular wasting show. It is more likely to be due to some chemical change, and this may be the presence of some substance foreign to the neuromuscular junction, or on the other hand some product of the destruction of acetylcholine, the removal of which is impaired. This latter possibility would seem a fruitful line for investigation, because prostigmin in large doses in normal muscle can have a depressant effect on rapid stimulation of the nerve, presumably due to accumulation of excess of transmitter (Briscoe, 1936). If this is so, then the retention of a breakdown product of acetylcholine, normal or otherwise, might produce a curare-like effect. The presence of large amounts of choline are known to raise the threshold for acetylcholine excitation experimentally, so that it is quite possible that an abnormal balance between production and removal of acetylcholine may be the basis of the defect in neuromuscular transmission. Study, therefore, of the actual nature of the chemical abnormality at the neuromuscular junction is a primary consideration in the further investigation of myasthenia gravis, but it must be remembered that the cause of this abnormality may arise from pathological changes outside the muscular system, and this leads to further consideration of the relationship of thymus hypertrophy to the disease.

Using dogs, Adler (1937) states that he has produced experimentally muscular weakness resembling clinical myasthenia by repeated transplants of thymus tissue from young animals. The symptoms so produced were completely relieved by prostigmin. Injections of thymus extracts also produced muscular weakness. Adler suggests that the enlarged thymus produces some substance which leads to an abnormal breakdown in acetylcholine at the myoneural junction. It is not likely that the explanation is so straightforward as this, because such a substance would be present in the serum, and the values for blood esterase would be likely to be higher instead of lower than normal.

If this work is confirmed it is clearly of very great importance, because it will enable a local disturbance at the myoneural junction at least analogous to that present in myasthenia gravis to be investigated experimentally. Details of the experiments and also the method of preparation of the thymic extracts are unfortunately not published. Rowntree *et al.* (1936) in their large number of experiments with injections of extracts of thymus and also transplants into rats did not record any muscular weakness in the experimental animals. Also Asher and Scheinfinkel (1929) claim to have separated two fractions in watery extract of thymus gland, one alcohol-soluble which relieves fatigue in muscle and the other alcohol-insoluble which accelerates growth in young rats. It may quite well be that different animals react differently to the thymus transplants, but clearly Adler's work must be repeated and extended.

Obiditsch (1937) has studied histologically a series of nine thymus tumours, and has found that those consisting of small round cells were associated with myasthenia symptoms, while those with epithelial and malignant cells were not. It is not known yet whether the pathological changes occurring in myasthenia gravis with thymic hypertrophy are the same as those occurring in thymic tumours with myasthenia, but they must be very closely related. Also Stern (1937) has described the recovery of a case of myasthenia gravis following the combination of prostigmin and irradiation of the thymus. He quite admits that the recovery may only have been a spontaneous remission, but clearly it is possible that irradiation combined with prostigmin may be effective, whereas the results from this treatment previously were inconclusive. Surgical removal of abnormal thymus tissue should also be considered in suitable patients.

There are some isolated observations in regard to myasthenia gravis which are interesting in their possible relationship either to the local abnormality at the neuromuscular junction or to the possible general pathological changes. It is known that thyroid extract in large doses produces temporary benefit followed by aggravation of the disease. The initial benefit may be due to increased metabolism at the neuromuscular junction, and as thyroid extract leads to thymus hypertrophy in animals the aggravation may be secondary to such a change. Injections of thymus extracts (Allen and Hanbury) have been observed to produce aggravation of symptoms in some cases (personal observation). Other observations clearly related to endocrine changes are the occurrence of remissions of the disease in association with pregnancy, and Simon (1935) has stated that improvement can be produced by treatment with anterior pituitary. On the other hand, potassium chloride in large doses (Laurent, 1936) and Veratrine (Kroll, 1936) produce beneficial effects in the disease, and the action of these drugs most probably takes place at the myoneural junction. The intolerance of myasthenic patients for large doses of local anæsthetics such as novocaine is probably also a direct effect of the drug at this junction.

Familial Periodic Paralysis

In this disease, which is most frequently familial but may be sporadic, attacks of muscular weakness varying in severity up to complete paralysis occur in otherwise healthy individuals. The paralysis, which may last many hours before complete recovery takes place, is rarely fatal from respiratory failure, and is associated with loss of deep reflexes and electrical inexcitability of the muscles.

Although the pathogenesis of the disease has remained obscure, it has been generally considered as most likely due to general metabolic disturbances of a temporary nature producing in some way a loss of muscular function. The results of recent chemical investigation in cases of the disease support this conception and indicate the lines of research along which a full explanation of the disease is likely to be found. The most important aspect of these investigations is the observation, to which attention was first directed by Allott (1935),

that a marked lowering of the serum potassium occurs during an attack. Aitken and Allott *et al.* (1937) showed that this could be produced by the administration of large amounts of glucose by mouth, by the injection of insulin, and more easily by both these procedures together. Allott and McArdle (1938) have extended these observations. They found that the potassium is not excreted during the attack and must therefore accumulate in some tissues and that the serum inorganic phosphate shows parallel variations to the potassium, only slighter in degree. Adrenaline also reduces the serum potassium and inorganic phosphate and may sometimes produce an attack. The normal serum potassium is 16–20 mg. per cent. and the level at which paralysis occurs is usually 10–12 mg. per cent., but in one case weakness developed with the potassium content just below 16. Administration of large doses of potassium citrate or potassium chloride cuts short the attack. How the paralysis arises from these chemical alterations is not clear. The fall in serum potassium is not the only factor, because by repeated adrenaline injections in a normal person the serum potassium can be lowered to a figure which would be associated with paralysis in a patient subject to these attacks, and very low figures have also been observed in diabetics under treatment with insulin without symptoms. As glucose and insulin administration normally gives rise to a slight fall in serum potassium, it would appear that in this disease an abnormal mobility of this ion exists with some phase of carbohydrate metabolism, so that potassium is removed not only from the serum but also from some part of the motor unit where its presence is necessary for the transmission of the nerve impulse or the excitation of the muscle. The inability of nerve or muscle to retain the necessary potassium concentration when abnormal metabolic variations occur may be the essential abnormality in the disease.

The main site of the lesion, if such it might be called, is probably in the muscle fibre distal to the nerve ending, because the paralysed muscle is inexcitable to direct electrical stimulation, though at present it is impossible to exclude simultaneous involvement of nerve.

Earlier observations in the disease are interesting in view of the more recent work. Shinosaki (1925) had observed in his cases that the administration of glucose and insulin and also adrenaline could precipitate attacks, but he did not correlate these observations with alteration in the potassium content of the serum. Biemond and Daniels (1934), on the other hand, recorded a lowered potassium content of the serum in one of their cases during an attack, the full significance of which they did not, however, appreciate ; and more recently Herrington (1937) has used therapeutically repeated 5-gm. doses of potassium citrate with very beneficial effects. Also some of the clinical features of the disease, such as precipitation of the attacks by excitement or their nocturnal occurrence after a late heavy meal, or the ability to avert attacks by exercise, can be considered as producing alterations in adrenaline output or carbohydrate metabolism and thereby correlated with the known chemical alterations in the disease. Another interesting feature of the disease is the fact that muscular atrophy sometimes supervenes. Biemond and Daniels (1934), while regarding the atrophy in their cases as neural in origin, held that it also was hereditary,

and not a secondary effect of the attacks because it bore no constant relationship to the number and severity of preceding attacks. It has not, however, as yet been definitely established that the wasting is neural or dystrophic in origin, a point of considerable interest in the classification of the disease.

Muscular Weakness and Hyperthyroidism

It is well known that in exophthalmic goitre muscular weakness is a prominent symptom, so much so that weakness of the quadriceps muscle has been recognized as a test for myasthenia in hyperthyroidism. It is significant that in exophthalmic goitre there is hyperplasta of the thymus and lymphorrhages have also been found in the muscles. Further, the full clinical picture of myasthenia gravis is not infrequently associated with exophthalmic goitre (Cohen and King, 1932), and the improvement in the muscle function following ephedrine and prostigmin leaves no room for doubt regarding the diagnosis. It is not likely that such an association is merely fortuitous, but rather that the hyperthyroidism has predisposed in susceptible individuals, possibly through the thymus hyperplesia, to the development of the pathological changes which constitute the disease of myasthenia gravis. Sauerbruch (quoted Adler, 1937) has removed a hyperplastic thymus gland from a patient with exophthalmic goitre and severe myasthenia. There followed a gradual disappearance of the myasthenia but no alteration in the thyrotoxicosis. The minor degrees of muscular weakness found in exophthalmic goitre probably depend on closely related if not identical pathological changes.

This leads to the consideration of exophthalmic ophthalmoplegia to which Brain (1937) has recently drawn special attention. The condition is characterized by opthalmoplegia of varying degree and sometimes œdema of the eyelids associated with thyrotoxicosis. The degree of thyrotoxicosis is usually slight and the condition may occur after thyroidectomy for hyperthyroidism when the basal metabolic rate is normal or even subnormal. Œdema of the orbit and enlargement of the ocular muscles has been observed at operation. Histologically the muscles show œdema with foci of lymphocytic infiltration, while fibrosis and enlargement of fibres have been reported. Prostigmin in such cases has no effect on the ocular movements, so that the condition is not the simple association of myasthenic symptoms of the ocular muscles with hyperthyroidism. Also the ophthalmoplegia does not appear to be entirely mechanical and due to the exophthalmos, because decompression may relieve the exophthalmos but not the muscular weakness. It has frequently been suggested that the thyrotropic hormone of the pituitary may play some part in the development of the condition, and recent experimental work supports this view. Smelser (1937) has injected extracts of the anterior pituitary into thyroidectomized guinea-pigs and has produced exophthalmos and œdema of the retrobulbar connective tissue, fat, and muscles indistinguishable from that found in clinical exophthalmos. There was also some round cell infiltration in the fat and muscles, but the degeneration of the latter was less than has been reported in clinical exophthalmos with hyperthyroidism. No reference was made to ophthalmoplegia in this work, but it would appear

from it that the exophthalmos in exophthalmic goitre and exophthalmoplegia are closely related.

How the thyrotropic hormone acts in the production of the exophthalmos and the lesions in the muscles is obscure. The muscle changes can, however, be regarded as a toxic myopathy secondary to metabolic abnormalities and they are probably responsible for the ophthalmoplegia, although mechanical alterations may accentuate the defects of movement. It is interesting that some cases of exophthalmic ophthalmoplegia are associated with generalized muscular wasting. The nature of the changes affecting the limb musculature is not known, but it is probable that they are similar to those affecting the eye muscles, and should also be regarded as a toxic myopathy of metabolic origin. Cases of muscular wasting occur, however, without ophthalmoplegia, so that comparison of the histological changes in the eye muscles and the limb muscles must be made before the two can be grouped together under the heading thyrotoxic myopathy.

Exophthalmic goitre is not only described in association with myasthenia gravis but also in association with periodic paralysis (Shinosaki, 1925 ; Dunlap and Kepler, 1931 ; Morrison and Levy, 1932). There is, however, generally an absence of a family history of the disease. Owing to the fact that in Dunlap and Kepler's patients thyroidectomy cured the attacks, the association of the two diseases cannot be regarded as fortuitous. Shinosaki (1925) has observed that the administration of thyroid extract may produce slight attacks in typical familial periodic paralysis. It would appear, therefore, that exophthalmic goitre can predispose in susceptible individuals to the development of pathological alterations similar to those occurring in this disease. The investigation of how these changes are brought about and also whether the attacks are accompanied by a fall in the serum potassium will be of great interest in regard to the pathogenesis of familial periodic paralysis.

Classification of Primary Diseases of Voluntary Muscle

The following classification of primary diseases of voluntary muscle is appended as a brief summary of the review. It is based on an attempt to assess the site and nature of the pathological changes responsible for the loss of function in each disease. Few, if any, of the complex problems presented by these diseases have been settled, but fruitful lines of investigation based on sound physiological and biochemical knowledge have been opened up, and it can confidently be expected that the future will show great advances in this field.

(1) Progressive muscular dystrophy.

Primary degeneration of the contractile elements of the muscle fibre. Nature entirely obscure.

(2) Dystrophia myotonica.

Primary degeneration of the muscle fibre closely allied to that in the first disease, with an added abnormality at the myoneural junction giving rise to myotonia.

(3) Myotonia congenita (Thomsen's disease) and myotonia acquisita.

Primary abnormality at the myoneural junction resulting in myotonia and secondary hypertrophy of the muscle fibre. Pathological physiology still obscure.

(4) Myasthenia gravis.

Essential lesion at the myoneural junction, but probably conditioned by pathological changes in the body generally.

(5) Familial periodic paralysis.

Essential lesion in the paths of excitation distal to the nerve ending. Associated with general metabolic abnormalities involving the potassium ion.

(6) Muscular disorders related to disease of the thyroid gland.

(*a*) Muscular hypertrophy and myotonic-like symptoms associated with hypothyroidism (rare).

(*b*) Myasthenia and occasionally the full clinical picture of myasthenia gravis complicating exophthalmic goitre.

(*c*) Periodic paralysis complicating exophthalmic goitre (rare).

(*d*) Thyrotoxic myopathy (rare). Weakness and wasting of voluntary muscles, probably dependent on toxic changes of metabolic origin affecting the muscle fibre. Associated with hyperthyroidism. Here may be grouped exophthalmic ophthalmoplegia as the changes in the muscle are also indicative of a toxic process.

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NOTICE

A RESEARCH BUREAU FOR PSYCHIATRY

Thanks to the generosity of the Rockefeller Foundation a bureau to aid research in psychiatry and allied subjects has been opened at 11, Chandos Street, under the auspices of the Royal Medico-Psychological Association. The bureau is primarily intended to aid research work in mental hospitals and institutions from which access to libraries and academic centres is difficult. Bibliography of recent literature together with abstracts of important papers on any particular subject relating to psychiatry and neurology will be supplied to applicants. Workers who may desire advice as to technical methods or any experimental difficulties will receive special advice, and if necessary be put into communication with authorities on the specific methods in question. Small grants may be made by the Committee of the Research Bureau to allow workers who might need such assistance to spend a few days at a specific laboratory or institution, where they could receive personal advice on their work and discuss their difficulties with experts. Technical handbooks are lent to workers who might otherwise have difficulty in obtaining them.

At intervals critical reviews of subjects of psychiatrical and neurological interest will be prepared and submitted in the first instance to journals for publication, and those for which no room can be found will be manifolded and sent to workers who express a wish to receive such reviews on any particular subject. The services of the bureau are gratuitously at the disposal of all workers in psychiatry and allied subjects who, owing to special circumstances, are in need of help.

EPITOME OF CURRENT JOURNALS

ACTA PSYCHIATRICA ET NEUROLOGICA

Vol. 12. Part 2. 1937.

Is it Probable that the Sociological Situation is a Factor in Schizophrenia? T. Braatöy. 109.

Untersuchungen bezgl. Senkungsreaktion bei Dementia Paralytica. (The sedimentation rate in general paresis.) K. H. Fremming and J. Madsen. 139.

The Mirror Sign. A Rather Neglected Symptom in Certain Mental Diseases. H. Knöös. 155.

Über den Wert der Liquorzuckerbestimmung in der Meningitis-diagnostik und einige Bemerkungen Über die postalimentäre Hyperglykorachie bei akuten Infektionskrankheiten. (The value of the examination of sugar in the cerebrospinal fluid in the diagnosis of meningitis, with some remarks on the post-alimentary sugar-content of the cerebrospinal fluid in acute infective diseases. N. I. Nissen. 173.

Considerations Inspirées par les Examens Successifs Pratiqués dans Environ 400 Cas d'Epilepsie. (Conclusions drawn from the successive examination carried out in about 400 cases of epilepsy.) H. S. Jögren. 185.

Syphilis des Nervensystems bei Asiaten in Niederländisch-Indien. (Neuro-syphilis in Asiatics in the Dutch Indies.) P. M. van Wulfften Palthe. 207.

Einige Untersuchungen über die Proteinsysteme der Cerebrospinal-flüssigkeit. (Investigations into the proteins of the cerebrospinal fluid.) A. Yde. 257.

Vol. 12. Part 3. 1937.

*Untersuchung über die Durchmesser und Querschnittflächen der Achsenzylinder in den Spinalnervenwurzeln des Menschen. (Examination of the diameter and cross-section areas of the axis cylinder in the spinal nerve roots of man.) N. Arnell. 287.

Über die Bedeutung des Partuspræmaturus für Entstehung gewisser zerebraler Affektionen. (The importance of premature birth as a cause of certain cerebral affections.) T. Brander. 313.

*Cerebral Changes in an Acute Case of Fat-Embolism. J. Cammermeyer. 333.

Dementia Paralytica Juvenilis. (Juvenile general paresis.) J. Ström. 355.

Cross-section Areas of the Axis-Cylinder.—The number of fibres in the anterior and dorsal roots of man have been counted and graded according to the thickness of the axis-cylinder. Also the number of non-myelinated fibres have been counted. In the anterior roots there is a great increase, actual and relative, of the larger nerves in lower cervical and lumbar roots. In the dorsal roots the largest fibres do not predominate in these regions, but the fibres of a slightly smaller size do. (E. A. C.)

Cerebral Changes in Fat-Embolism.—A careful study has been made of changes in the cortex and white matter of the brain in a subject who died 29 hours after fat-embolism. Importance is given to the capillary network and its field of distribution as an explanation of the site and character of lesions found. (E. A. C.)

Vol. 12. No. 4. 1937.

Aphasieprobleme. (The Problem of Aphasia.) H. Torp. 397.

Les Troubles Intellectuels dans l'Aphasie et les États Similaires. (Mental disturbances in aphasia and similar states.) T. Lindqvist. 411.

Neurochirurgische Kasuistik zur Aphasiefrage. (Neuro-surgical case reports on the question of aphasia.) E. Busch. 429.

*Contribution à la Localisation de l'Agraphie. (Contribution to the localization of agraphia.) H. Marcus. 431.

The Method of Examination in Amusia. H. J. Ustvedt. 447.

Faseranalytische Studien über die Pyramidenbahn. (Studies of the fibres of the Pyramidal Tracts.) G. Haggqvist. 457.

Experimental Investigations of the Associated Connections of the Cerebral Cortex, with Special Reference to the Conditions in the Frontal Lobe. J. Jansen. 467.

Untersuchungen über die verschiedenen Funktionen der Skelettmuskulatur mit spezieller Berücksichtigung ihres anatomische Substrats. (Enquiry into the various functions of the musculature of the skeleton, with special reference to its anatomy.) G. Wohlfahrt. 469.

Giving Advice in Questions of Education and Upbringing: A New Form of Neuro-Prophylaxis. T. Ramer. 471.

Neuere Untersuchungen über "Encephalomyelitis funicularis infectiosa." (Recent investigations into infective "Encephalomyelitis Funicularis.") C. J. Munch-Petersen. 477.

Die extraduralen Knochengeschwülste des Spinalkanals. (The extradural bone tumours of the spinal canal.) E. Christensen and E. Busch. 481.

*Die hypothalamische Lokalisation der histologischen Befunde in Korsakowfällen. (The hypothalamic localization of the histological findings in cases of Korsakow's syndrome.) St. Környey and H. Saethre. 491.

Über die Behandlung der Chiasmagliome. (The treatment of gliomas of the chiasma.) E. Busch. 499.

Tumors in the Third Ventricle of the Brain. A. Torkildsen. 501.

Das Encephalogramm bei Encephalopathia trau-

matica. (The encephalogram in "Encephalopathia Traumatica.") E. Mindus. 505.
Über einige Fälle von "Encephalopathia anæmica." (Some cases of "Encephalopathia Anæmica.") R. Bringel. 507.
Syndrome s'accompagnant d'Acinésie "Frontale." (A syndrome associated with "frontal" akinesia.) R. Almqvist. 515.
Glycine Effect in Myopathies. R. Forsberg. 529.
Ein Fall von sensorischer Aphasie und Leukämie. (A case of sensory aphasia and leukæmia.) H. Torp. 531.
*Epilepsy and Alimentary Glycæmia. H. I. Schou. 533.
Vaso-Vagale Synkope und orthostatische Epilepsie. (Vaso-vagal syncope and orthostatic epilepsy.) N. Antoni. 545.
Gesichtspunkte über ein Material von 400 Fällen von Epilepsie. (A study of 400 cases of epilepsy.) H. S. Jögren. 561.
*Epileptic Fits provoked by Means of Monobromated Camphor. H. Lilliestierna. 563.
Elektrodenzahlenbestimmungen. (Examination with electrodes.) T. B. Wernoe. 571.
*Visceral Pain experimentally produced from Œsophagus. G. K. Stürup. 577.
Über die Behandlung der Trigeminusneuralgie peripherer Natur. (The treatment of trigeminal neuralgia of peripheral origin.) B. Grundt. 585.
La Névrite Tardive du Cubital et son Traitement Chirurgical par Transposition Ante-Épitrochléenne du Nerf. (Neuritis of the cubital nerve and its surgical treatment by transposition.) H. Jessen. 597.
Continued Investigations into the Diastase Content of the Ventriculo-Subarachnoideal Cavity compared with that of the Blood Serum. H. Christiansen. 599.
Automatische graphische Registrierung des Liquordruckes. (Automatic graphic recording of the cerebrospinal fluid pressure.) S. Lagergren. 605.
Studien an spinalen Blockfällen, mit Berücksichtigung der Diffusion im Liquorraum. (Studies of cases of spinal block, with special reference to the diffusion into cerebrospinal fluid space.) S. Zetterholm. 607.
Formation of Crystals in the Spinal Fluid. Zeiner-Henriksen. 620.
*On Queckenstedt's Test. M. Fog and J. Ravn. 627.
Über die Grösse der Liquorsekretion bei Menschen. (The amount of cerebrospinal fluid secretion in man.) O. Sjöqvist. 635.
Nervous Sequelæ of Spinal Anæsthesia. G. Rørvig. 637.
*On Four Cases of Leucodystrophia Cerebri Hereditaria Progressiva. R. Forsberg and R. Stromme. 639.
Über die Inkubationszeit bei der künstlichen Malaria. (The incubation period of artificial malaria.) T. Østrem. 643.

The Localization of Agraphia.—A good clinical description of a case is given along with a careful anatomical study. The author comes to the conclusion that the destruction of the second frontal convolution was the cause of the agraphia. (E. A. C.)

Histological Findings in Cases of Korsakow's Syndrome.—A short pathological description of three cases diagnosed as having the symptoms and signs of Korsakoff's syndrome. Much attention is paid to possible changes to be found in the hypothalamus. (E. A. C.)

Epilepsy and Alimentary Glycæmia.—Attention is drawn to certain changes in the blood-sugar curve in patients with epilepsy. He believes that an alimentary hypoglycæmia exists in nearly 40 per cent. of all epileptics. This defect is only to be found in curves over a period of 4 hours. In the later hours a hypoglycæmia to below 40 mgm. per cent. may occur, and it is usual for the attacks to take place about this time. (E. A. C.)

Epileptic Fits and Monobromated Camphor.—The administration of camphor monobrom by mouth in doses of 0·20 to 0·25 gm. with a total daily dosage up to 2·25 gm., produced an epileptic attack in 27 cases of epilepsy. In 23 other cases who had not previously had epilepsy only one had an attack. (E. A. C.)

Visceral Pain from Œsophagus.—The sensations associated with distension by one or two balloons in the œsophagus are described. Sensation was frequently localized to the epigastrium, sometimes to the substernal region and occasionally to the pharynx. Cooling and warming the area of skin in the region where the sensation was felt caused no alteration in the pain, but affected the peristalsis. Anæsthetization of the skin was also undertaken and caused a change in the character of the pain. (E. A. C.)

Queckenstedt's Test.—Using Queckenstedt's test during manometric readings of lumbar fluid pressure and comparing the results with those obtained on abdominal straining the authors have found that variations which occur may give a clue to the presence of a cerebral tumour. (E. A. C.)

Four Cases of Leucodystrophia.—The clinical conditions in four members of the same family are recorded and a diagnosis made of Pelizaeus-Merzbucher's disease. No histological evidence is available to uphold this diagnosis. (E. A. C.)

AMERICAN JOURNAL OF PSYCHIATRY

Vol. 93. No. 6. May 1937.

Intelligence and Socialization. F. L. Wells. 1,265.
*Blood Estrin Level in Schizophrenia. H. A. Sears, R. A. Morter, M. Simonson, and C. Williams. 1,293.
Luetic Hypertrophic Hepto-Meningitis. A. P. Smith. 1,305.
Brain Potential Rhythms in a Case showing Self-Induced Apparent Trauma States. M. M. Thomson, T. W. Forbes, and M. M. Bolles. 1,313.
The Response of Psycho-Neurotics to Variations in Oxygen Tension. R. A. McFarland and A. L. Barach. 1,315.
The Science of Man. A. Korzybski. 1,343.
Psychosis with Cardiac Decomposition. J. C. Michael. 1,353.
An Evaluation of Opposed Theories concerning the Ætiology of So-Called "Dementia" in Dementia Præcox. M. P. Wittenau. 1,363.
*Prefrontal Leucotomy in the Treatment of Mental Disorders. E. Moritz. 1,379.

Clinical Staff Conference. C. F. Read. 1,391.
The Case of Floyd Dell. A Study of the Psychology of Adolescence. L. J. Bragman. 1,401.
The Influence of Carbon-Dioxide in combating the Effect of Oxygen Deficiency on Psychic Processes, with Remarks on the Fundamental Relationship between Psychic and Physiologic Reactions. E. Gallhorn. 1,413.
The Correlation of Oxygen-Deprivation with Intelligence, Constitution, and Blood Pressure. S. H. Kraines. 1,435.
*On the Relationship of the Sudden Withdrawal of Alcohol to Delirium Tremens. P. Piker. 1,387.

Blood Estrin Level in Schizophrenia.—By means of the Frank and Goldberger test the authors have shown that 69·35 per cent. of the schizophrenic female subjects have no demonstrable quantity of blood estrin. In 50 normal menstruating women only 8 per cent. showed this. (E. A. C.)

Prefrontal Leucotomy in Mental Disorders.—The author, by means of cutting the brain in various sites with the aid of a special knife, deduces that he has obtained good results in subjects with symptoms of mental upset. He believes that recovery on account of this treatment may take place. (E. A. C.)

Withdrawal of Alcohol in Delirium Tremens.—The author offers observations which indicate that delirium tremens is not caused or prolonged by the abrupt withdrawal of alcohol. (E. A. C.)

Vol. 94. No. 1. July 1937.

A Note on the Urinary Phosphate of Night Urine in Mental Disease. W. M. Bachinski and J. J. Rae. 19.
*The Effect of Benzedrine Sulphate on Certain Abnormal Mental States. P. G. Schube, M. C. McManamy, C. E. Trapp, and A. Myerson. 27.
Definition of Childhood in Psychiatric Literature. C. Bradley. 33.
*Six Years' Experience with Narcosis Therapy in Psychiatry. H. D. Palmer and F. J. Braceland. 37.
Hyperthyroidism and Personality. W. T. Brown and E. F. Gildea. 59.
The Significance of Special Reading Disability in Mentally Handicapped Problem Children. T. G. Hegge. 77.
*Symposium on Therapy including Hypoglycæmia :
The Psychiatric Manifestations of Hypoglycæmia. E. J. Kepler and F. P. Moersch. 89.
The Methodical Use of Hypoglycæmia in the Treatment of Psychoses. M. Sakel. 111.
Report of the Hypoglycæmic Treatment in New York State Hospitals. J. H. Ross. 131.
Experience with the Hypoglycæmic Treatment of Schizophrenia. S. Katezenelbogen, H. Harms, and D. A. Clark. 135.
Further Experiences at Bellevue Hospital with the Hypoglycæmic Insulin Treatment of Schizophrenia. J. Wortis, K. M. Bowman, L. L. Orenstein, and I. J. Rosenbaum. 153.
Experiences with the Hypoglycæmic Shock Treatment of Schizophrenia. J. A. Young, R. H. Young, and L. Roucek. 159.
The Effect of the Hypoglycæmic Therapy on the Psychotic Process. B. Glueck. 171.
The Problem of Insulin Shock. H. J. John. 175.
The Encephalogram of Schizophrenics during Insulin Treatment. H. Hoagland, D. E. Cameron, and M. A. Rubin. 183.

Benzedrine Sulphate in Abnormal Mental States.—The administration of benzedrine caused no improvement in a number of cases of major psychoses. In 15 of the 80 cases studied the psychosis was temporarily accentuated.

Narcosis Therapy in Psychiatry.—This is a valuable article in which the authors have carefully studied the effects of narcosis therapy. Consideration has been given to the physiological effects. By this method it sometimes became possible to get into close contact with the patient, but the results in schizophrenia were disappointing. It is useful in the treatment of the manic depressive group, especially in the acute manic attacks.

Symposium on Therapy including Hypoglycæmia.—These are a series of papers dealing with the various aspects of this form of therapy. They cover a wide range and give a general view of the present situation regarding insulin therapy.

Vol. 94. No. 2. September 1937.

The Campaign against Epilepsy. William G. Lennox. 251.
*Prognosis in Mental Disease. The Use of One-Page Abstracts. Earl D. Bond and Francis J. Braceland. 263.
The Society, the Individual, and His Mental Disorders. W. Lloyd Warner. 275.
Exogenous Reaction Types in Brucella Infection. (Undulant fever.) B. M. Serafimov. 285.
The Care of Extramural Patients with Major Convulsions. David C. Wilson. 293.
*A Review of 140 Cases of Affective Disorders—after Seven Years. Leslie B. Hohman. 303.
Age Incidence of Dentia Paralytica. Magnus C. Petersen. 309.
Emotional Responsiveness in Clinical Reviews. John C. Whitehorn. 311.
Some Psychiatric Aspects of Birth Control. Sarah P. Kelman. 317.
Lunacy and the Moon. Carl E. Trapp. 339.
Nursing Education. May Kennedy. 345.
*The Irritative Treatment of Schizophrenia. Review of 20 Cases. Emerick Friedman. 355.
Herpes Zoster following Lumbar Puncture. A Case Report. H. R. Carter. 373.
Present Crisis in Social Relationships. Samuel W. Hartwell. 379.
The Effect of the Stimulus Word used upon Scores in the Association-Motor Test. Newell C. Kephart and H. Max Houchens. 393.
The Disclosure of Foster-Parentage to a Boy. Sidney Tarachov. 401.

Prognosis in Mental Disease.—The authors present five-year follow-up studies for all patients admitted consecutively between 1927 and 1928 to the Pennsylvanian Hospital. Of the 710 admissions, 84 cases were not considered as they were not of psychiatric interest. For 626 consecutive cases the results after five years were—recovery : 200 ; improved : 102 ; unim-

proved : 106 ; death : 129 ; lost : 48. These cases included every category of psychosis. Of 116 cases of dementia præcox, 12 recovered and 25 were improved. The authors strongly advocate the use of "one-page abstracts" made out on the back of the ordinary case records.

Outcome in Affective Disorders.—The author studied the symptomatology, course and outcome of 144 cases of affective psychosis, which represent all the cases of this nature seen by him during 1929. In 137 cases there were 85 recoveries within one year, 23 within two years, 10 in the third year, and 19 after three years. From this study the author concludes that the Kraepelinian concept of manic depression is valuable as indicating that the more pervasive the affect the greater the chance of spontaneous recovery, and that admixtures of symptoms belonging to the organic psychoneurotic or paranoid groups of reaction tend to militate against recovery.

Irritative Treatment of Schizophrenia.—Twenty cases of schizophrenia were treated by the use of convulsive drugs. In 11 cases the convulsant drug employed was camphor, in seven Metrazol, and in two cases both were employed. The selection of drugs was arbitrary. Fifteen cases improved sufficiently to be allowed to go home, but not sufficiently for discharge, and three were unimproved. Three of the cases treated had been affected for over three years. Two of these improved.

ANNALES MEDICO-PSYCHOLOGIQUES

Vol. 11. No. 4. November 1937.

Recherches sur la Surface de l'Écore Cerébrale. (Research on the surface-area of the cerebral cortex.) P. Nayrac and G. Fournier. 581.

*Les Aptitudes Intellectuelles Spéciales chez les Instables. (The special intellectual capabilities of unstable children.) J. Abramson. 603.

Evolution d'une Catonie Pure chez une Jeune Malade de 17 Ans. (Evolution of catatonia in a young patient aged 17 years.) M. Brissot and J. Maillefer. 632.

Psychose Réactionelle à Forme de Délire de Compensation chez un Isréalite Allemand Exilé. (Reaction psychosis in the form of compensation delirium in a German Jewish exile.) P. Courbon and M. Leconte. 686.

Psychose Présénile et Arterio-Sclérose Cerébrale à Forme Mentale. (Presenile psychosis and cerebral arteriosclerosis with mental symptoms.) L. Marchand and G. Demay. 646.

La Therapeutique Convulsante de la Psychose Manio-Depressive. (Convulsant therapy of the manic-depressive psychosis.) P. Verstraeten. 654.

A Propos du Mode d'Action de l'Insuline et du Cardiazol dans la Therapeutique de la Schizophrenie. (On the action of insulin and cardiozol in the therapy of schizophrenia.) H. Bersot. 659.

Psychose Addisonnienne : Essai de Traitement Chloruré. (Addisonian psychosis : attempted chloride treatment.) A. Porot. 665.

Psycho-encephalite à Pousseés Successives, caracteriseé par des Accidents Convulsifs. (Psycho-encephalitis with successive exacerbations characterized by convulsive symptoms.) Porot and Bardenat. 669.

Paralysie Générale chez la Mère et Fille : Précession de la Maladie chez l'Enfant. (General paralysis in mother and daughter : earlier onset in child.) Porot, Bardenat, and Sutter. 674.

Confusion Mentale apres une Injection de Serum Anti-Tétanique : Accident du Travail : Invalidité. (Mental confusion following an injection of anti-tetanic serum.) Ledoux, Desruelles, and Gomet. 678.

Un Cas de Psychose de Korsakoff avec Ulcère Perforant et Pleurésie à la Suite d'une Intoxication par l'Héroine. (A case of Korsakoff psychosis with a perforating ulcer and pleurisy as a result of heroin intoxication.) A. Repond. 684.

Debilité Mentale et Paralysie Générale Infanto-Juvenile : A Propos d'un Cas de Paralysie Générale Juvenile à Debut Épileptique chez un Hérédo-Syphilitique. (Feeblemindedness and infantile general paralysis : a report of a case of congenital general paralysis starting epilepsy in an hereditary syphilitic.) H. Roger and J. Alliez. 687.

Polio-Encephalite de Wernicke avec Délire Hallucinatoire d'Origine Ethylique : Guerison des Troubles Bulbo-Protuberantiels. (Polio-encephalitis with hallucinations of alcoholic origin : cure of bulbar symptoms.) H. Roger, J. Paillas, and P. Laval. 694.

Intellectual Capabilities of Unstable Children.—This paper forms the second of a series of studies on the psychology of the mentally unstable child. The children examined were aged from 13 to 18 years ; most of them being between 15 and 17. Out of 2,212 children brought to the clinic for infantile neuropsychiatry, 50 per cent. showed signs of instability and about one child in four was considered to be a case of psychomotor instability. It is on this group of 531 children that most of the observations were made. Studies on the memory power and observation, imagination, and attention of these children have led to the conclusion that attention is the most greatly affected faculty. In less than 2 per cent. of the cases was this faculty found to approach normality. The power of logical reasoning is more or less affected in 53 per cent. of the cases. Inventivity and imagination are below the average in 42 per cent. of the children. On the other hand primitive and unorganized memory, that is, memory more or less independent of attention and reasoning processes, is practically normal. The power of concrete observation of inanimate objects seems to be unaffected in these unstable children.

ARCHIVES OF NEUROLOGY AND PSYCHIATRY

Vol. 38. No. 1. July 1937.

*Vascular Architecture of the Lesions of Multiple Sclerosis. T. J. Putnam and Alexandera Adler. 1.
Relationship of the Autonomic Nervous System to Pathogenesis of Epilepsy. K. Orzechowski. 16.
*Lissauer's Dementia Paralytica : A Study of its Pathogenesis. N. Malamud. 27
*Combined System Disease in Tabes Dorsalis. C. Davison and H. Kelman. 43.
*Unsteadiness of the Heart Rate in Psychotic and Neurotic States. J. C. Whitehorn and Helen Richter. 62.
Aggression and Anxiety in the Determination and Nature of Manic Attacks. N. L. Anthonisen. 71.
*Stain for Myelin Sheaths in Tissues embedded in Paraffin. G. S. Mahon. 103.
Unilateral Cerebral Dominance as related to Mind Blindness : Minimal Lesion capable of causing Visual Agnosia for Objects. J. M. Nielsen. 108.
Contribution to the History of Narcolepsy. H. A. Cave. 136.

Vascular Architecture in Multiple Sclerosis.—A study of the changes in vascular architecture and the spatial relationships of blood vessels to sclerotic plaques showed that small plaques tend to surround engorged veins, which are gnarled and tortuous. If a thrombus occurs in a vein, an area of fresh degeneration appears in close relation to it. There is usually an increase of capillaries in sclerotic plaques, but a decrease may also occur. (R. M. S.)

Lissauer's Dementia Paralytica.—From a study of four cases of Lissauer's dementia paralytica the author concludes that the specific histological picture of the lesions, namely, status spongiosus and its tendency to laminal distribution, is conditioned by colloidal (synäretic) changes of exogenous origin. (R. M. S.)

Combined System Disease in Tabes.—The authors consider that the combination of lesions of the pyramidal tract and posterior column sometimes seen in tabes dorsalis are produced by the direct action of toxic substances on the lateral and posterior columns of the cord. (R. M. S.)

Heart Rate in Psychotic and Neurotic States.—The principal conclusion to be drawn from these observations is that psychotic patients, even when reacting with so-called affective behaviour in a personal interview, maintain a steadiness of heart rate greater than that of normal subjects, whereas neurotic patients tend towards a greater unsteadiness of heart rate. (R. M. S.)

Stain for Myelin Sheaths.—Mahon describes a staining method for myelin sheaths in formalin-fixed, paraffin-embedded material. The technique does not require mordanting of the blocks or differentiation of the sections after staining. It is not applicable to frozen sections. (R. M. S.)

Vol. 38. No. 2. August 1937.

Prognostic Factors in Spontaneous Subarachnoid Hemorrhage. I. Strauss and S. Tarachow. 239.
*Epileptiform Convulsions from " Remote " Excitation. F. A. Fender. 259.
*Cystic Tumor of the Third Ventricle containing Colloid Material. H. Zeitlin and B. W. Lichtenstein. 268.
*Experimental Studies of Serum Lipase in Multiple Sclerosis. K. C. Swan and H. B. Myers. 288.
*Relation of the Hypothalamus to Disorders of Personality. Report of a Case. B. J. Alpers. 291.
Survival and Revival of Nerve Centres following Acute Anemia. C. Heymans, J. J. Bouckaert, F. Jourdan, S. J. G. Nowak, and S. Farber. 304.
Effect of Experimental Lesions of the Cortex on the " Psychogalvanic Reflex " in the Cat. H. G. Schwartz. 308.
*The Cerebral Circulation. XXXL. Effect of Alcohol on Cerebral Vessels. Caroline B. Thomas. 312.
*Effect of Injections of Colloidal Thorium Dioxide on the Ventricles and Subarachnoid Spaces. W. Freeman. 340.
*Psychoses associated with Pernicious Anæmia. M. Herman, H. Most, and N. Jolliffe. 348.
Method for Rapid Impregnation of Microglia and Oligodendroglia in Material fixed in Formaldehyde. L. S. King with the assistance of J. Anderson. 362.
Continuous Records of Systolic and Diastolic Blood Pressure. C. W. Darrow. 365.
*Functional Determinants of Cerebral Localization. K. S. Lashley. 371.

Epileptiform Convulsions from " Remote " Excitation.—The author describes a method of producing epileptiform convulsions in dogs that allows observation of the complete attacks in unanæsthetized, unrestrained subjects. These convulsions, which appear to approach those seen in clinical epilepsy more closely than experimental convulsions ordinarily produced by electrical stimulation, are described in detail. (R. M. S.)

Cystic Tumour of the Third Ventricle.—Clinical and pathological observations are reported in two cases of cystic tumour of the third ventricle of the brain containing colloid material. The authors consider that the structures observed within the cyst are identical with those present in the paraphysis of the human embryo and of lower vertebrates, thus substantiating the theory that this cyst is a derivative of the embryonic structures of the paraphysis. It is suggested that this type of tumour of the third ventricle be named paraphysial cyst. (R. M. S.)

Serum Lipase in Multiple Sclerosis.—Repeated determinations made over a period of 9 months in the serums of nine patients with multiple sclerosis revealed no substantial evidence to support the concept that abnormal lipolytic activity of the serum is present in this disease. (R. M. S.)

Relation of the Hypothalamus to Disorders of Personality.—A mild-mannered, even-tempered man developed during his illness periods of depression, alternating at times with periods of unmotivated excitement, easily elicited reactions of rage with loss of inhibitory reactions in general. Death occurred 8 days after a transfrontal craniotomy. Histological studies of a dermoid found in the third ventricle revealed severe damage of the nuclei of the hypothalamus, except for the nucleus mamillo-infundibularis. The author considers that damage to these areas was responsible for the changes in personality observed in this case. (R. M. S.)

The Cerebral Circulation.—The experiments described in this paper demonstrate that alcohol consistently causes dilatation of the pial arteries of cats and rabbits and is independent of changes in the systemic arterial pressure, which may fall, rise, or remain unchanged. Alcohol invariably produces a rise in cerebrospinal fluid pressure, and increases the flow of blood through the brain. During arterial dilatation the flow of blood through the pial veins becomes visibly more rapid, and the colour of the vein changes from blue to red. These findings suggest that dilatation occurs in other cerebral arteries and arterioles, as well as in the pial arteries. (R. M. S.)

Injections of Thorium Dioxide.—A study of two specimens obtained for biopsy and material from eight autopsies showed that the injection of colloidal thorium dioxide as an agent for ventriculography may condition pathological changes. This agent exerts a transitory inflammatory reaction in the choroid plexus, ependyma, and meninges. In cases of ventricular obstruction profound inflammatory changes may ensue, with suppurative ependymitis, desquamation of the ependyma, and formation of plaques and masses of thorium in phagocytes on the denuded surface of the ventricles. (R. M. S.)

Psychoses in Pernicious Anæmia.—The mental picture in psychotic patients with pernicious anæmia does not show any characteristic or diagnostic content. In order of frequency the types of mental reaction are : an acute confusional state, a paranoid condition, an affective reaction, and an organic deterioration type. The acute confusional state occurring during a relapse of the anæmia is a serious complication and should be treated by blood transfusions until the establishment of a blood response by specific therapy. (R. M. S.)

Vol. 38. No. 3. September 1937.

*Hypothalamic Regulation of Temperature in the Monkey. S. W. Ranson, C. Fisher, and W. R. Ingram. 445.
*Anterolateral Chordotomy for Intractable Pain of Tabes Dorsalis. E. A. Kahn and B. F. Barney. 467.
*The Psychopathology of Pick's Disease. K. Goldstein and S. E. Katz. 473.
Word Association as affected by Deficient Oxygen, Excess of Carbon Dioxide, and Hyperpnea. E. Gellhorn and S. H. Kraines. 491.
*Involutional Melancholia : Treatment with Theelin. P. G. Schube, M. C. McManamy, C. E. Trapp, and G. F. Houser. 505.
*Effect of Roentgenotherapy on Gliomas. I. M. Tarlov. 513.
Poliomyelitis (Poliomyelopathia) Chronica : Report of a Case, with Histologic Study. Albert T. Steegmann. 537.
*Connections between the Striatum and the Substantia Nigra in a Human Brain. R. Wayne Rundles and J. W. Papez. 550.
*Changes in the Spinal Cord in Diabetes Mellitus : Report of a Case with Autopsy. D. E. Griggs and C. W. Olsen. 564.
Repression and Communicability in Catatonic Stupor. B. Cohen. 572.
The Cerebellum : A Review and Interpretation. O. Larsell. 580.

Hypothalamic Regulation of Temperature in Monkey.—Experimental lesions in the hypothalamus may cause either transient hyperthermia or more prolonged hypothermia. In monkeys with hypothermia the lesions were observed to have extended backward to the level of the mamillary nuclei, while in those with hyperthermia the lesions were confined to the rostral part of the hypothalamus. The lesions in these animals were placed bilaterally in the lateral part of the hypothalamus and seldom involved the walls of the third ventricle, but the possibility that medially placed lesions might produce the same results has not been excluded. Recovery from hyperthermia usually occurred within 24 hours. Hypothermia lasted many days, but disappeared as a rule within a month. Even after the hypothermic monkeys had recovered sufficiently to maintain normal body temperature under ordinary room conditions, they were still unable to compensate normally for high or low room temperatures. (R. M. S.)

Anterolateral Chordotomy for Pain in Tabes.—The authors recommend that when standard methods of treatment fail to relieve the intractable pain of tabes dorsalis, the comparatively neglected procedure of anterolateral chordotomy should be tried. In at least eight of the twelve cases presented this procedure had relieved entirely the pain when the patient last reported. Brief histories in the twelve cases mentioned, together with treatment and the results of operation, are recorded. (R. M. S.)

Psychopathology of Pick's Disease.—The fact that atrophy in Pick's disease involves especially the frontal lobes emphasizes the importance of a search for symptoms which are considered to be characteristic of lesions of the frontal lobe. This is most likely to be successful at the onset of the disease, when the personality has not yet changed to such a degree that good co-operation and

an exact examination are impossible. The writers describe special tests for: (1) behaviour to space; (2) behaviour to time; (3) perception; (4) movements; (5) following directions; (6) recognition; (7) reading aloud; (8) speech. (R. M. S.)

Involutional Melancholia.—Theelin was administered to ten persons with involutional melancholia. In these ten patients there was no improvement or recovery. The condition of seven patients remained unchanged; in three the psychosis was aggravated during the treatment and the physical condition became more grave. Theelin was of no value in treatment in the cases of involutional melancholia studied. (R. M. S.)

Roentgenotherapy in Gliomas.—Medulloblastoma was the only glioma in the series studied in which there was convincing evidence of a uniformly beneficial effect of roentgenotherapy. (R. M. S.)

Connections between Striatum and Substantia Nigra.—Microscopic examination of a complete series of Pal-Weigert sections through the brain stem of an American writer and lecturer revealed bilateral degeneration of the caudate nucleus and the putamen, with preservation of the globus pallidus. It is therefore possible to follow independently the efferent fibres leaving these nuclei. The striatum, including the caudate nucleus and the putamen, has direct fibre connections with the globus pallidus and, what is equally important, also with the substantia nigra. The ansa lenticularis, the fasciculus lenticularis, and the pallidosubthalamic tract contain no fibres of striate origin. Symptomatology referable in individual cases to either striatum or to the substantia nigra is explained on the basis of an interruption of this strionigric relationship. Cortical projections to the centrum medianum and the arcuate nucleus of the dorsal thalamus are described. (R. M. S.)

Spinal Cord Changes in Diabetes Mellitus.—A case of diabetes mellitus exhibiting symptoms typical of involvement of the posterior and lateral columns of the spinal cord is reported. Since these portions of the cord are supplied by the longest penetrating arteries, the authors think it possible that narrowing of the lumens incident to thickening of the walls of the vessels reduces the blood supply to these regions and thus produces the characteristic funicular necrosis. (R. M. S.)

ARCHIV FÜR PSYCHIATRIE UND NERVENKRANKHEITEN

Vol. 106. No. 6. July 1937.

Ergebnisse der Fiebertherapie der progressiven Paralyse an der Münchener Psychiatrischen und Nervenklinik. (Results of fever therapy in general paralysis at the Munich Mental Hospital.) H. Reker. 617.
*Über einen Fall von Hemiballismus. Beitrag zur Somatotopie des Corpus Luysi. (A case of hemiballismus. The problem of localization of function in the corpus Luysii.) A. Juba and E. Rakonitz. 624.
Zur Frage der Beeinflussbarkeit schizophrener Störungen. (The susceptibility to influence in schizophrenic disturbances.) W. Jahrreis. 643.
Über die Bedeutung des "mittleren feldes" der Kolloide des Liquors. (The significance of the middle field in colloidal curves of the spinal fluid.) P. Büchler. 654.
Über die verschiedenen Insulinshocktypen und ihre neuropsychopathologische Bedeutung. (Various types of insulin shock and their significance.) L. v. Angyal. 662.
Zur Frage der Encephalomyelitis post vaccinationem. (The problem of post-vaccinal encephalitis.) L. Suppan. 681.
Gibt es symptomatische Psychosen bei Urämie? (Are there symptomatic psychoses in uræmia?) P. H. Esser. 698.
Ein Fall von Nucleus Ruber Läsion. (A case of lesion of the red nucleus.) R. Stähli. 710.
*Über ein periodisch auftretendes Syndrom: Steigerung der Speichelsekretion, parkinsonistische Motilität, melancholische Depression. (A periodic syndrome with salivation, Parkinsonism, rigidity, and melancholic depression.) E. Stengel. 726.
*Klinisches Bild und anatomischer Befund nach Drosselung. Ein Beitrag zur Frage der örtlichen Vulnerabilität. (Clinical and pathological findings in strangulation. The problem of relative vulnerability.) E. Gamper and G. Stiefler. 744.
Schädigungen des Nervensystems bei Serumkrankheit. (Nervous disturbance in serum disease.) N. Schipkowensky. 779.

A Case of Hemiballismus.—In 18 cases of hemiballism collected from the literature the corpus Luysii was clearly the substrate of the condition. The case of the authors is a new contribution which confirms the somatotopic conception of Santha, who ascribed movements of the head and face to lesions of the frontal part, those of the trunk and extremities to the caudal part of the centre. (A. M.)

A Periodic Syndrome with Parkinsonism.—The author describes cases of encephalitis epidemica (one case in full) in which temporary attacks of increased oliguria, sweating, salivation, Parkinsonian rigidity, hypersomnia, and melancholic episodes were observed. In the case reported in full these attacks lasted several weeks. In other patients a similar syndrome was seen as accompaniment of short oculogyric crises. The vegetative and motor phenomena seen in such attacks resemble physical phenomena accompanying typical melancholic phases of the manic-depressive group. According to the author the periodicity of all these phenomena is essentially determined by the sleeping mechanism to which close regional relationship within the diencephalon exists. (A. M.)

Problem of Relative Vulnerability.—De-

tailed clinical and pathological report on a case showing neurological symptoms after strangulation : A boy, æt. 16, was strangled for 20 seconds. After a healthy interval of 4 days acute deterioration developed with signs of a mixed pyramidal and extrapyramidal lesion. Pathological examination revealed ischemic changes in the cortex, particularly the third layer of the premotor and motor region and in the striate body. The globus pallidus was intact. In the discussion the authors deal with the selectivity of the lesions and the pathogenesis of the delayed onset. They are struck by the localization of the lesions in regions with a motor function. This susceptibility of the motor system is supported by clinical and experimental observations of Wagner-Jauregg and H. Strauss. The delayed onset can be explained by the deteriorating effect of the resumption of function upon a tissue which has been impaired by the original anoxæmia. This is in agreement with experimental results recently published by Buechner and Luft. The regional selectivity may be determined by specific properties of the capillaries in different regions. Thus the conception of pathoclisis can be reconciled with a vascular theory. (A. M.)

Vol. 107. No. 1. September 1937.

Manifestationswahrscheinlichkeit und Erbgang der Schizophrenia. (Heredity and probability of manifestation in schizophrenia.) V. Ziehen. 1.
Zum Liquorsyndrom des Rückenmarktumors. Mit einem Nachtrag Bemerkungen zu den Liquorveränderungen bei den Hirngeschwülsten. (Cerebrospinal fluid findings in spinal tumours, with an appendix on cerebral tumours.) A. Bannwarth. 61.
Über einere bioelektrische Reaktionen der "optischen" Hirnrinde und zur Frage ihrer Zuordnung zu Wahrnehmungen. (Bioelectric phenomena in the visual cortex and their significance with regard to perception.) A. E. Kornmüller. 93.
Dementia Paralytica bei genuiner Epilepsie. (General paralysis in true epilepsy.) M. Lieber. 106.
*Über Kleinhirnveränderungen bei tuberöser Sclerose und zentraler Neurofibromatose. (Cerebellar changes in tubero-sclerosis and central neurofibromatosis.) W. Ammerbacher. 113.
Über die Zirkulationsgeschwindigkeit des Blutes bei Geisteskranken. (Velocity of the blood circulation in mental disorder.) D. T. Dimitrijevic. 142.
Die verschiedenen Lebensabschnitte in ihrer Auswirkung auf das psychiatrische Krankheitsbild. (Age and its influence on mental disorder.) A. Boström. 155.
Epilepsie im ersten Lebensjahrzehnt. (Epilepsy in the first decade of life.) J. Lange. 172.
*Über örtliche Veränderung der Konfiguration des Gehirns bei Hirndruck. (Zisternenverquellung und Verschiebung über die Mediæbene.) (Local disfiguration of the brain in intracranial pressure. "Cisternal swelling" and displacement over the middle line.) T. Hasenjäger and H. Spatz. 193.

Cerebellar Changes in Tubero-Sclerosis.—The cerebellum is more often affected in cases of tubero-sclerosis than it was recognized previously. In nine personal cases it was invariably involved though to a varying degree. The changes can be classified into ventricle tumours, cortical nodules alike those in the cerebrum and general disturbances of development (heterotopic nests of ganglion cells and spongioblasts, neuroblastic appearance of ganglion cells, misshaped and misplaced Purkinje cells). The well-known relationship of tubero-sclerosis to central neurofibromatosis is particularly marked in the cerebellum. The onset of the lesion is later in the cerebellum than in the cerebral cortex. (A. M.)

Disfiguration of the Brain in Intracranial Pressure.—The careful and well-illustrated paper deals with circumscribed disfiguration of the brain due to swelling of certain convolutions. Since this happens particularly in the neighbourhood of the cisternæ, the authors speak of "cisternal swelling," which term is used instead of the older term "cerebral hernia" (Adolf Meyer). In cases of unilateral tumours cisternal swelling is often associated with a displacement of the midline structures towards the contralateral side. The falx of the dura and the stalk of the hypophysis remain, however, in their place. The swelling of the cisterna interhemispherica can be seen by means of ventriculography and arteriography (arteria cerebri anterior). Cisternal swelling as well as the displacement of the median structures may give rise to focal symptoms which must not be ascribed to the tumour itself. (A. M.)

BRAIN

Vol. 60. No. 3. July 1937.

*Vasomotor Responses in the Toes : Effect of Lesions of the Cauda Equina. J. Doupe, J. S. M. Robertson, and E. A. Carmichael. 281.
*Dural Sinus Thrombosis in Early Life : Recovery from Acute Thrombosis of the Superior Longitudinal Sinus and its Relation to Certain Acquired Cerebral Lesions in Childhood. O. T. Bailey and G. M. Hass. 293.
*Abnormalities in the Amount and Circulation of the Cerebrospinal Fluid associated with Otitis Media. A. A. McConnell. 315.
*The Syndrome of the Superior Cerebellar Peduncle in the Monkey. A. E. Walker and E. H. Botterell. 329.
*Ataxia and Astereognosis of Bulbar Origin. M. David and H. Askenasy. 354.
Cerebral Infection with "Schistosoma Japonicum." J. G. Greenfield and B. Pritchard. 361.

Vasomotor Responses in Toes.—Vasoconstrictor responses in the toes and fingers to various stimuli were recorded plethysmographically. In normal subjects

responses were more readily elicited in the toes than in the fingers. Stimuli applied to the legs or venous congestion of the legs tended to accentuate this difference. In subjects with lesions of the cauda equina the toe responses were parallel to those in the finger. Therefore the toe vessels constrict more readily because of afferent impulses arising in the legs. (J. D.)

Dural Sinus Thrombosis.—Three cases of superior longitudinal sinus thrombosis in childhood are reported in which death did not occur for several months. After the initial acute illness there was a degree of recovery followed by mental deterioration, associated with hydrocephalus and epilepsy. Autopsy showed organized canalized thrombi in the superior longitudinal sinuses. In two cases there was a vascular hæmorrhagic thickening of the meninges over the convexity of the hemispheres, while the other case showed a small area of necrosis in the frontal lobe, probably due to venous thrombosis. Sinus thrombosis may play a part in the pathogenesis of focal cerebral gliosis and subdural and subarachnoid hæmorrhage. (J. D.)

Amount and Circulation of C.S.F. associated with Otitis Media.—Following otitis media an abnormality in either the amount or the circulation of the c.s.f. may develop. The latter complication is exemplified by three cases of localized cystic collection of normal c.s.f. under moderate tension in the posterior fossa and one case of fluid encysted in the ventricles by fibrinous adhesions in the region of the foramen of Magendie. A case of communicating hydrocephalus is reported to illustrate an abnormality in amount of c.s.f., and a case of compensatory hydrocephalus occurring in an individual with otitis media is also reported. Lumbar puncture is contra-indicated in encysted collections of fluid, whether they are purulent or not. Ventricular puncture is safe and aids in the differential diagnosis. An excess of subarachnoid fluid indicates an external, probably communicating, hydrocephalus. A large ventricle suggests the lesion to be in the posterior fossa, while a small ventricle may mean a cyst in the temporal lobe. (J. D.)

Superior Cerebellar Peduncle.—Baboons and macaques were subjected to section of one or both superior cerebellar peduncles. The resulting ipsilateral ataxia was attributed to interruption of the brachium conjunctivum. Bilateral section produced a more profound and bilateral ataxia involving the trunk as well as the limbs. There was no evidence of lamination in the brachium conjunctivum. Nystagmus and hypotonia were transient and insignificant in degree, while spontaneous tremors did not occur. (J. D.)

Ataxia and Astereognosis of Bulbar Origin.—During removal of a hæmangioblastoma the nuclei of Goll and Burdach were damaged. The patient subsequently showed marked ataxia, hypotonia, and loss of position sense. The reflexes were normal, as was appreciation of heat, cold, and pain. (J. D.)

L'ENCEPHALE

Année 32. Vol. 2. No. 2. July 1937.

Recherches sur les Polypeptides du Sang et du Liquide Céphalo-Rachidien dans les Maladies Mentales. (Investigations on the polypeptides of the blood and cerebrospinal fluid in mental illnesses.) H. Claude, J. Dublineau, and H. E. and Mlle. Bonnard. 57.

L'Influence du Système Végétatif Central sur les Fonctions Psychiques Normales et Pathologiques. (The effect of the autonomic nervous system on normal and abnormal mental function.) M. Monnier. 75.

Sur la Fatigabilité dans la Sclérose en Plaques. (On fatigue in disseminate sclerosis.) D. Noica. 96.

Année 32. Vol. 2. No. 3. September 1937.

*Le Mécanisme de la Mort dans Certains Cas de Tumeur Cérébrale. (The mechanism of death in certain cases of cerebral tumour.) P. van Gehuchten. 113.

Habitus Acromégalique et Perversion Sexuelle. (Acromegaly and sexual perversion. A case analysis.) F. Morel. 128.

Cerebral Tumour.—Six cases of sudden or rapid fatal termination of the course of cerebral tumour. Death followed lumbar puncture in one, ventrigulography in two, and decompression in three. In five cases the tumour was temporal in situation and in all there was herniation of the medial aspect of the temporal lobe through the tentorial opening. The temporal lobe thus compresses the peduncular region and the pons. In all cases perivascular hæmorrhagic foci were found in the regions, without evidence of rupture of vessels. The authors find the hæmorrhagic foci to be due to local diapedesis around arterioles and discuss its possible mechanism. (D. D.-B.)

JAHRBÜCHER FÜR PSYCHIATRIE UND NEUROLOGIE, WIEN

Vol. 54. No. 3. December 1937.

Über eine disseminierte und diffuse Angiose des Zentralnervensystems. (Disseminated and diffuse angiosis of the central nervous system.) E. Pollak. 246.
Frontalsyndrome und Parietooccipitalsyndrome. (Syndromes of the frontal and parietooccipital region.) G. Bychowsky. 283.
Handschrift und Geisteskrankheit. (Handwriting and psychosis.) K. Gross and M. Bauer-Chlumberg. 312.

Angiosis of the Central Nervous System.—In a man of 60 a state of spastic paraplegia with severe disturbance of micturition and defæcation developed slowly and lead to death from bronchopneumonia and cystopyelitis. There was a diffuse overgrowth and collagenous thickening of the vessels in the lower brain stem beginning at a high cervical level and extending up to the middle third of the pons. A similar change was found in a circumscribed area in the right temporal lobe. There were hæmorrhages and a partial destruction of nervous tissue, presumably secondary to the teleangiectasis and to the changes of the vessels and connective tissue in the teleangiectatic areas. Vascular anomalies of the same character but of a much smaller degree were to be seen extending downwards to the conus terminalis of the spinal cord. The author regards the disease as a true tumour formation. (K. S.)

JOURNAL OF ANATOMY

Vol. 71. No. 4. July 1937.

On the Nature and Mode of Origin of the Foramen of Magendie. J. J. Wilson. 423.
Some Observations on the Major Subdivision of the Marsupialia. A. A. Abbie. 429.
Cor Biloculare, with a Note on the Development of the Pulmonary Veins. F. Davies and M. A. MacConaill. 437.
*The Course of Fibres in the Dorsal Nerve Roots of "Macaca Mulatta," the Rhesus Monkey. J. Z. Young and S. Zuckerman. 447.
Normal Facial Growth in Children. M. Young. 458.
Growth of Cartilage Canals in the Patella. R. W. Haines. 471.
*Continuity in Nerve Fibres. H. H. Woollard. 480.
The Lymphatics of the Stomach. J. H. Gray. 492.
The Innervation and Morphology of the Cervical Intertransverse Muscles. A. J. E. Carr. 497.
The Fœtal Growth of the Sheep. H. A. Harris. 516.
A Preliminary Communication upon the Cerebral Commissures of the Mammalia. G. Elliot Smith. 528.

Fibres in the Dorsal Nerve Roots of the Rhesus Monkey.—In 14 monkeys the dorsal roots were severed central to the ganglia and the animals killed 15–22 days later. At most five degenerating fibres were found in any one root adjacent to that which had been divided. No such degenerating fibres were found in roots more distant. These observations have been discussed in relation to the work of Barron and Matthews. (E. A. C.)

Continuity in Nerve Fibres.—Evidence is submitted that plexuses occur at the body's surface which may involve continuity between adjacent nerve fibres. In rabbits there is actual visual evidence of the continuity of the neurofibrils in the plexus and the final endings emerge from the fibrils of the terminal plexus. In man this continuity is found only in the fine subepidermal plexus. (E. A. C.)

Vol. 72. No. 1. October 1937.

Studies on the Area Vasculosa of the Embryo Chick. II. The Influence of the Circulation on the Diameter of the Vessels. A. F. W. Hughes. 1.
The Relation between the Size of the Artery and the Capillary Bed in the Embryo. H. H. Woollard and J. A. Harpman. 18.
*The Development of the Cerebro-Spinal Fluid Spaces and Choroid Plexus in the Chick. H. Cohen and S. Davies. 23.
*The Nerve Supply of Bone. D. J. Hurrell. 54.
*Cultivation of Nerve Cells "in vitro" over a Long Period. H. Meyer and W. Jablonski. 62.
The Torus Mandibularis in the Bushman. M. R. Drennan. 66.
The Suprarenals of the Larger Felidæ. W. C. Osman Hill. 71.
Congenital Urogenital Anomalies in Rats, including Unilateral Renal Agenesia. A. M. Hain and E. M. Robertson. 83.
Variations from Normal Gait after Muscle Section in Rabbits. D. Stewart. 101.
The Development of the Penile Urethra and the Homology of Cowper's Gland of Male Spermophile, with a Note on the Prostatic Utricle M. A. H. Siddiqi. 109.
*A Simple Apparatus for stimulating Human Nerves. V. Y. Inman and R. C. Combs. 116.
On Subcutaneous Veins of the Neck. E. Pikkieff. 119.
A Valved Transverse Septum in the Femoral Vein. A. G. Gibson and K. J. Franklin. 128.

Cerebrospinal Fluid Spaces.—By means of injection of fluid into the central nervous system or into the vascular system of chick embryos it has been possible to demonstrate that the choroid plexus develops first in the third and lateral ventricles. The choroid plexus of the fourth ventricle matures at a later date. The authors have found that the spread of cerebrospinal fluid occurs at the same time as the development of the choroid plexus. (E. A. C.)

Nerve Supply of Bone.—A method is described which permits of staining nerve

fibres in bone. With this method the author has confirmed de Castro's observation that most of the nerves in bone go to blood vessels. Some fibres were found to end blindly in the bone matrix and others in close relation with the bone cells. (E. A. C.)

Cultivation of Nerve Cells.—The authors amplify their earlier observations on the cultivation of spinal ganglia of chicken embryos. Cultures have survived for 19 weeks. They found no increase in the number of ganglia cells and no migration of these into the zone of mesenchyme cells. Very clear neurofibrillæ could be observed in the cells during life and without fixation or staining. In the older cultures the cells vary in shape, become lobular, and have fine long excrescences. (E. A. C.)

Apparatus for Stimulating Human Nerves.—A simple apparatus for stimulating peripheral nerves in the human is described. (E. A. C.)

JOURNAL BELGE DE NEUROLOGIE ET DE PSYCHIATRIE

Vol. 37. No. 7. July 1937.

A Propos du Régime des Malades Mentaux dans qualques Pays d'Europe. (Regulation of care of mental diseases in some European countries.) F. Nyssen. 411.

*Contribution à l'Étude Clinique et Anatomique de l' " Atrophie Cérébelleuse Tardive à Prédominance Corticale." (Contribution to the clinical and anatomical study of delayed cortical cerebellar atrophy.) A. de Haene. 427.

Tumeur Développée dans le Canal Optique. (Tumour originating in the optic foramen.) C. Vincent and E. Hartmann. 455.

Delayed Cortical Cerebellar Atrophy.—Male, aged 60, with ataxic gait of 18 years' duration and slight difficulty in articulation. Nystagmus was present. Swallowing unaffected. No tremor. No ataxia of upper limbs until late in the disease. Gait reeling, titubant, and grossly ataxic. Congenital absence of left sixth nerve. Atrophy of oral extremity of the inferior olive and of the palæocerebellum. No affection of the pons or other parts of the brain. Disappearance of the climbing fibres, as well as the Purkinje cells in the affected cerebellar cortex. It is concluded that the climbing fibres arise in the olive. A rôle in the ætiology is attributed to alcohol in this case. (D. D.-B.)

Vol. 37. No. 8. August 1937.

Syndrome Catatonique Expérimental Produit par le Cardiozol. (Catatonia produced by cardiozol.) Leroy, A. and P. Clémens. 487.

Compression Médullaire par Varices de la Pie-Mère. (Spinal compression by varices.) Andersen and R. Dellaert. 499.

Produit Incesteueux dans une Famille Comportant Trois Générations de Débiles Mentaux. (Incest in a family covering three generations of mental defect.) A. Ley. 504.

Contribution à l'Étude du Liquide Céphalo-Rachidien des Déments Précoces Spécialement en ce qui Concerne la Chlorurrachie. (A study of cerebrospinal fluid in early dementia.) G. Muyle. 509.

Vol. 37. No. 9. September 1937.

Les Caractères Anatomiques Généraux des Maladies Hérédo-Famiales du Système Nerveux. (The general anatomical characteristics of heredofamilial nervous diseases.) C. Schaffer. 543.

*Sur Quelques Causes d'Aggravation Rapide et de Mort Subite dans les Syndromes d'Hypertension Intracranienne. (Some causes of rapid aggravation and sudden death in intracranial hypertension.) M. David and H. Askenasy. 550.

Vaste Hématome Sous-Dural chez un Paralytique Général. Plaques Séniles Disséminées dans le Cortex. (Large subdural hæmatoma in a general paralytic. Senile plaques in the cortex.) P. Divry. 566.

Méningiome Intracérébelleux. (Intracerebellar Meningiomata.) L. Christophe and P. Divry. 575.

Hémangiomes Caverneux Vertébraux avec Syndrome de Compression Médullaire. (Cavernous cerebral hæmangioma with spinal compression.) W. Zawadowski and J. Jarzymski. 583.

Considérations sur un Cas de Parkinsonisme Associé aux Symptômes de Diabète Sucré. (On a case of Parkinsonism associated with diabetes mellitus.) M. Cahane and T. Cahane. 598.

Intracranial Hypertension.—Herniation of the temporal lobe through the opening of the tentorium cerebelli is as common as pressure cone at the foramen magnum. Differential diagnosis and treatment is discussed. (D. D.-B.)

JOURNAL OF CLINICAL INVESTIGATION

Vol. 16. No. 4. July 1937.

The Effect of Heating with Alkali on the Calorigenic Activity of Desiccated Thyroid and of Thyroxine. W. O. Thompson, P. K. Thompson, S. G. Taylor, and L. F. N. Dickie. 479.

Manganese Metabolism in Health and Disease :

I. The Magnesium and Calcium Excretion of Normal Individuals, also the Effects of Magnesium, Chloride, and Phosphate Ions. D. M. Tibbetts and J. C. Aub. 491.

II. The Effect of the Parathyroid Hormone. D. M. Tibbetts and J. C. Aub. 503.

*III. In Exophthalmic Goiter, Basophilic Ad-

enoma, Addison's Disease, and Steatorrhea. D. M. Tibbetts and J. C. Aub. 511.
Studies in Temperature Sensation :
*I. A Comparison of the Sensation produced by Infra-Red and Visible Radiation. T. W. Oppel and J. D. Hardy. 517.
*II. The Temperature Changes Responsible for the Stimulation of the Heat End Organs. T. W. Oppel and J. D. Hardy. 525.
III. The Sensitivity of the Body to Heat and the Spatial Summation of the End Organ Responses. J. D. Hardy and T. W. Oppel. 533.
Acute Mountain Sickness : The Effect of Ammonium Chloride. E. S. Guzman Barron, D. B. Dill, H. T. Edwards, and A. Hurtado. 541.
The Use of Ferrous Gluconate in the Treatment of Hypochromic Anemia. P. Reznikoff and W. F. Goebel. 547.
Rheumatic Fever as a Familial Disease. Environment, Communicability, and Heredity in Their Relation to the Observed Familial Incidence of the Disease. M. G. Wilson and M. D. Schweitzer. 555.
Splenic Vein Pressure in Congestive Splenomegaly (Banti's Syndrome). W. P. Thompson, J. L. Caughey, A. O. Whipple, and L. M. Rousselot. 571.
Studies of the Principle in Liver Effective in Pernicious Anemia.
IV. The Therapeutic Activity of Its Multiple Factors. B. M. Jacobson and Y. Subbarow. 573.
Vitamin C Saturation Levels in the Body in Normal Subjects and in Various Pathological Conditions. P. Finkle. 587.
Studies on the Elastic Properties of Human Isolated Aorta. P. Hallock and I. C. Benson. 595.
Calcium and Phosphorus Metabolism in Osteomalacia. V. The Effect of Varying Levels and Ratios of Calcium to Phosphorus Intake on Their Serum Levels, Paths of Excretion and Balances, in the Presence of Continuous Vitamin D Therapy. S. H. Liu, C. C. Su, S. K. Chou, H. I. Chu, C. W. Wang, and K. P. Chang. 603.
Studies in Iron Transportation and Metabolism :
I. Chemical Methods and Normal Values for Plasma Iron and "Easily Split-off" Blood Iron. C. V. Moore, W. R. Arrowsmith, J. J. Quilligan, and J. T. Read. 613.
II. The Mechanism of Iron Transportation : Its Significance in Iron Utilization in Anæmic States of Varied Etiology. C. V. Moore, C. A. Doan, and W. R. Arrowsmith. 627.
The Result of Intra-Arterial Injection of Vasodilating Drugs on the Circulation : Observations on Vasomotor Gradient. E. V. Allen and G. R. Crisler. 649.
The Validity of the Calculation of Standard Urea Clearances from Low Urine Volumes. L. C. Chesley. 653.
*Proceedings of the Twenty-Ninth Annual Meeting of the American Society for Clinical Investigation held in Atlantic City, N.J., May 3, 1937. 657.

Basophilic Adenoma.—Among other subjects examined has been one suffering from a basophilic adenoma of the pituitary. Metabolic studies before and after X-ray treatment to the pituitary gland show that the previous loss of calcium was changed to a retention of calcium. (E. A. C.)

Infra-Red and Visible Radiation.—Radiation, as a form of stimulating temperature endings in the skin, has been studied. (E. A. C.)

Temperature Changes in Heat End Organs.—By methods described in the former paper its authors have produced evidence which suggests that stimulation of warm sensation depends upon a decrease of the normal thermal gradient in the skin and not on the degree or rate of temperature change in the skin. (E. A. C.)

Annual Meeting of American Society for Clinical Investigation.—Among many papers given the following are of interest :

(1) On the Mechanism of Migraine Headache and the Action of Ergotamine Tartrate. J. R. Graham and H. G. Wolff.

By optical methods amplitude of pulsation in branches of the external and internal carotids has been studied. Ergotamine tartrate caused a decrease in amplitude of temporal artery pulsation. The middle meningeal artery also showed constriction. The amplitude of intracranial arterial pulsation varied greatly following ergotamine.

(2) Effect of Pleasant and Unpleasant Mental Content upon the Respiratory Tracing (Spirogram) in Psychoneurotic Patients. J. E. Finesinger and S. Cobb.

It was found that pleasant ideas were associated with a decrease in rate of respiration and a decrease in amplitude while with unpleasant ideas the opposite were recorded. (E. A. C.)

Vol. 16. No. 5. September 1937.

Changes in the Vasomotor Reaction association with Glomus Tumors. Samuel J. Stabins, John J. Thornton, and W. J. Merle Scott. 685.
The Daily Urinary Excretion of Estrogenic and Androgenic Substances by Normal Man and Women. T. F. Gallagher, D. H. Peterson, R. I. Dorfman, A. T. Kenyon, and F. C. Koch. 695.
The Urinary Excretion of Androgenic and Estrogenic Substances in Certain Endocrine States. Studies in Hypogonadism, Gynecomastia, and Virilism. A. T. Kenyon, T. F. Gallagher, D. H. Peterson, R. I. Dorfman, and F. C. Koch. 705.
Nutritional Edema in the Dog. V. Development of Deficits in Erythrocytes and Hemoglobin on a Diet Deficient in Protein. A. A. Weech, M. Wollstein, and E. Goettsch. 719.
Loss of Minerals through the Skin of Normal Humans when Sweating is avoided. R. H. Freyberg and R. L. Grant. 729.
Adjustment of the Flow of Tissue Fluid in the Presence of Localized, Sustained High Venous Pressure as found with Varices of the Great Saphenous System during Walking. Henry K. Beecher. 733.
The Coagulation Defect in Hemophilia. The Effect in Hemophilia of Intramuscular Administration of a Globulin Substance derived from Normal Human Plasma. Frederick J. Pohle and F. H. L. Taylor. 741.
The Opsono-Cytophagic Test in Children with Pertussis and in Children vaccinated with H. Pertussis Antigens. Charlotte Singer-Brooks and J. J. Miller, Jr. 749.
Plasma Cholesterol Saturation in Patients with Hypertension. With a Note on Preparation of Glass Filters for Micro Filtration of Cholesterol Digitonide. R. F. Holden, Jr. 763.
Studies on the Mechanism of Proteinuria. E. H. Keutmann and S. H. Bassett. 767.
Studies in the Physiology of Blood Vessels in Man. Apparatus and Methods.
I. Sensitive Plethysmosphygmograph for a Portion of the Finger. R. H. Turner. 777.
II. A Method for the Determination of the Volume of the Soft Tissue about the Terminal Phalanx of the Human Finger. W. A. Sodeman. 787.
Studies in the Physiology of Blood Vessels in Man.
III. Some Effects of Raising and Lowering the

Arm upon the Pulse Volume and Blood Volume of the Human Finger-tip in Health and in Certain Diseases of the Blood Vessels. R. A. Turner, G. E. Burch, and W. A. Sodeman. 789.
A Clinical Study of the Action of 10 commonly used Drugs on Cardiac Output, Work, and Size : on Respiration, on Metabolic Rate, and on the Electrocardiogram. I. Starr, C. J. Gamble, A. Margolies, J. S. Donal, Jr., N. Joseph, and E. Eagle. 799.
The Opsono-Cytophagic Reaction of the Blood in Pertussis. W. L. Bradford and Betty Slavin. 825.
The Effect of Immune Blood upon the Opsono-Cytophagic Power of the Blood in Pertussis. W. L. Bradford, R. Mikell, and Betty Slavin. 829.

JOURNAL OF COMPARATIVE NEUROLOGY

Vol. 67. No. 2. August 1937.

*The Course of the Secondary Vestibular Fibres in the Cat. A. R. Buchanan. 183.
*Reaction of Spinal Canglion Cells to Section of Dorsal Roots. J. C. Hinsey, M. A. Krupp, and W. T. L. Hamon. 205.
*Regeneration of Nerves to the Adrenal Gland. W. H. Hollinshead and H. Finkelstein. 215.
*Experiments on the Origin of the Sheath Cells and Sympathetic Neuroblasts in Amphibia. C. P. Raven. 221.
*Trophic Control of Non-Nervous Tissues by the Nervous System : a Study of Muscle and Bone Innervation from an isolated and Quiescent Region of Spinal Cord. S. S. Tower. 241.
*Further Experimental Investigations on the Phenomenon of Homologous Response in Transplanted Amphibian Limbs. IV. Reverse Locomotion after the Interchange of Right and Left Limbs. P. Weiss. 269.
*Relationships of Thalamic Nuclei to the Cerebral Cortex in the Cat. W. H. Waller and R. W. Barris. 317.
Physiological and Morphological Regeneration of the Sectioned Spinal Cord in Adult Teleosts. H. Tuge and S. Hanzawa. 343.

Secondary Vestibular Fibres in the Cat.—Using a modified Horsley-Clarks stereotaxic instrument, discrete lesions were made with a unipolar electrode in the cerebellar nuclei of 14 cats ; 12–15 days later the entire central nervous system was stained by an adaptation of the Marchi technique. The contralateral ascending medial longitudinal fasciculus receives fibres from the medial nucleus and Deiter's nuclei ; the homolateral from the former and Bechterew's nucleus. The descending medial longitudinal fascicular carries fibres to the anterior funiculus from all the nuclei of both sides. These fibres terminate at different levels depending on their origins. The upper part of Deiter's nucleus sends ascending fibres in the homolateral tract of Deiter, while the lower part and Bechterew's give rise to fibres descending in the homolateral vestibulo-spinal tract. The ascending fibres terminate in relation to the motor ocular nuclei and collaterals appear to end in relation to the reticular cells of the medulla and pons. (J. D.)

Spinal Ganglion Cells in Dorsal Root Section.—The right hind limb of seven young cats were deafferented by section of the posterior roots. Comparative cell counts were made on the 4–5 L. and 2 S. ganglia of the right and left sides. Two animals were examined in 8 days and the remainder after 2–3 years. The 4–5 L. ganglia showed a variable decrease in cells after 2–3 years, accounted for by trauma and scarring. Otherwise there was no decrease in the number of cells after severance of their central connections and no evidence of regeneration of these connections. (J. D.)

Regeneration of Nerves to Adrenal Gland.—The adrenal gland of the cat was denervated by removal of the lower thoracic and upper lumbar sympathetic chain. There was evidence of regeneration at the third month and apparently normal innervation was established at the fourth month by fibres arising from the lower thoracic and upper lumbar spinal nerves. (J. D.)

Sheath Cells and Sympathetic Neuroblasts in Amphibia.—A piece of extoderm from the median part of the open neural plate of the embryo of amblystoma mexicanum was transplanted homotopically to triton tæniatus at the same stage of development. Differentiation of the post cells from those of the graft was made on the basis of size. In the course of a few weeks sympathetic neuroblasts and sheath cells of Schwann developed from the graft. This, together with previous work, showed that the sympathetic nervous system had origin both from the neural tube and from the neural crest. The sheath cells arise exclusively from the tube. (J. D.)

Trophic Control of Non-Nervous Tissues.—In three puppies the lumbo-sacral region of the spinal cord was isolated by transection above and below and by section of the posterior roots. Quiescence of the region was shown by nearly complete absence of muscle movement. The animals were sacrificed and studied histologically, 2, 5, and 6 months later. The skeletal muscles were atrophied and fibrosed. The fibres were reduced in size and stained poorly, but lacked the nuclear proliferation caused by degeneration. Therefore the trophic control of muscle requires both intact nerve supply and nervous activation. The bones developed normally in length and form but not in thickness or detail. These later are determined by muscle action. (J. D.)

Homologous Response in Transplanted Amphibian Limbs.—At an age when the limbs had been functionally differentiated for some months larval salamanders were subjected to an interchange of forelimbs, the left taking the place of the right and vice versa, so that a mirror image of the original arrangement was produced. Nerve

connection was established in 3–4 weeks. In walking progression was impossible as the forelimbs tended to propel the body backwards, each muscle of the transplant contracting at the same phase as would its synonymous muscle in the original limb. This condition persisted unchanged for over a year. Bone motor patterns are intrinsic properties of the central nervous system and in the salamander are incapable of being remodelled by peripheral influences. This contrasts with the situation in mammals. (J. D.)

Relationship of Thalamic Nuclei to Cerebral Cortex.—The thalamocortical connections in the cat were demonstrated by areas of degeneration in the thalamus following cortical lesions. (J. D.)

JOURNAL OF MENTAL SCIENCE

Vol. 83. No. 345. July 1937.

Mental Observation Wards. A Discussion of Their Work and Its Objects. E. U. H. Pentreath and E. C. Dax. 347.
Temporary Treatment. An Analysis of Thirty Cases. L. H. Wootton and L. Minster. 366.
Acetasol in the Treatment of Late Congenital Syphilis amongst Mental Defectives. K. C. L. Packer. 372.
Acrocyanosis. S. S. Stern. 408.
A Note on Some Vasomotor Disturbances in Schizophrenia. L. Minster. 437.
Scheme for the Examination of Organic Cases. W. Mayer-Gross and E. Guttmann. 440.
The Iron, Copper, and Manganese Content of the Human Brain. A. H. Tungay. 452.
An Undecided Compensation Claim arising from the Suicide of a Voluntary Patient. K. K. Drury and C. E. J. Freer. 461.
Syphilis in Mental Hospital Practice. D. Prentice. 472.

Vol. 83. No. 346. September 1937.

Some Observations on the Care of the Insane. D. McRae. 459.
Some Remarks on the Physiology of the Cerebral Circulation. F. L. Golla. 505.
The Histopathological Criteria of Vascular Disturbances in the Brain. A. Meyer. 509.
The Relative Vascularity of Different Areas of the Mammalian Brain. A. C. P. Campbell. 510.
Cerebral Ischemia and Mental Disorder. F. A. Pickworth. 512.
The Circulatory Factor in the Pathogenesis of Mental Disorder. E. Krapf. 534.
Psychological Implication of Functional Circulatory Disorder. E. Guttmann. 542.
Psychoses associated with Hypertension, Arteriosclerosis, and Heart Failure. W. Mayer-Gross. 551.

These papers were given during a Symposium dealing with the circulatory system and mental disorders. They do not lend themselves to abstraction.

Vol. 83. No. 347. November 1937.

Convulsion Therapy in Schizophrenia. A. Kennedy. 609.
*An Unusual Complication of Insulin Shock (Hypoglycæmic) Therapy. C. B. Molony and S. H. Honan. 630.
The Value of Continuous Narcosis in the Treatment of Mental Disorder. H. A. Palmer. 636.
Epileptic Reactions: an Attempt at Classification. A. Guirdham. 679.
*The Treatment of Epilepsy with Psychosis by Prominal. D. E. Sands. 703.
*Familial Psychosis associated with Endocrine Disorder. T. A. Munro. 707.
A Case of Profound Dissociation of the Personality. C. L. Copeland and E. Howard Kitching. 719.

Treatment of Epilepsy by Prominal.—A comparison was made between Prominal and phenobarbitone or bromides. In 15 cases Prominal was used alone, and combined with the other two drugs in 11 cases. All cases were psychotics with frequent fits. The general conclusions were that in no cases did the fits disappear, but that Prominal reduced the number of fits in the majority of cases, and that in patients showing less severe mental deterioration there was an improvement mentally and physically and in occupational capacity. With more advanced degrees of insanity phenobarbitone or bromides still give better results.

Complication of Insulin Shock Therapy.—A female patient undergoing insulin shock therapy on the twenty-second day of treatment did not awake from the hypoglycæmic coma on being given food. Intravenous glucose and adrenalin also failed to revive her. Blood and spinal fluid sugar contents were then shown to be excessive. An antidiabetic treatment, including insulin, was administered with success. For the first 20 days of the treatment no abnormal reactions had been noted. The amount of insulin, which began with 10 units, had been increased daily by about 5 units.

Familial Psychosis with Endocrine Disorder.—A sister and a brother aged 60 and 61 are described as suffering from psychosis characterized by a progressive emotional apathy leading to gross deterioration of conduct with loss of memory and lack of insight. The psychosis in the woman began about 15 years later than in the man. In both cases there were signs of endocrine dysfunction, hyperpiesia, hypertrichosis, with skin pigmentation in the woman and diminished sexual activity in the man. High blood cholesterol was found in the woman with an increase of red blood cells. The parents were first cousins.

JOURNAL OF NERVOUS AND MENTAL DISEASE

Vol. 86. No. 1. July 1937.

The Effect of Avertin Fluid (Tribromethanol) on the Brain Stem. R. R. White, R. T. Bellows, and W. P. van Wagenen. 1.

Polioencephalomyelitis due to Botulism. G. A. Schwarz. 7.

The Analysis of Mitogenetic Blood Radiation in Mental Disorder as a Basis for Therapy. S. Brainess. 24.

The Dictaphone as an Aid to Psychiatric Case Presentations. C. P. Oberndorf. 37.

Can a Reorientation through Mass Therapy correct the Fallacious Concept of the Incurability of Mental Disease? A. W. Hackfield. 39.

Vol. 86. No. 2. August 1937.

*The Relation of the Motor Area of Primates to the Hyporeflexia ("Spinal Shock") of Spinal Transection. J. F. Fulton and G. P. McCough. 125.

The Bible and Neurology in New Amsterdam. T. K. Davis. 147.

Exopthalmic Goiter and Psychosis. I. Bram. 152.

Fever Treatment of Dementia Præcox with Sulphur-in-Oil. L. B. Shapiro. 162.

Mirror Behaviour in Schizophrenic and Normal Individuals. S. Rosenzweig and D. Shakow. 166.

The Analysis of Mitogenetic Blood Radiation in Mental Disorder as a Basis for Therapy (*concluded*). S. Brainess. 175.

Spinal Shock.—Using chimpanzees and four species of monkeys the duration of depression of reflexes of the hind-limb following unilateral ablation of the motor area was studied. It was found that the greater the cortical development the longer was the period of depression and that reflexes involving the distal part of the extremity were more profoundly affected than those of the proximal segments. This was contrasted with the condition following spinal transection or hemisection, in which the proximal reflexes were the more affected. When spinal transection was performed after the cortical ablation or spinal hemisection the duration of "spinal shock" was shorter on the previously paretic side. This, however, was not true if sufficient time had elapsed between operations for compensation to occur. It was noted also that reflex activity was not depressed for several minutes following transection. The causes of the ultimate deterioration of reflex activity in the spinal monkey were studied. (J. D.)

Vol. 86. No. 3. September 1937.

Art and Therapy in the Mental Disturbances of Children. L. Bender. 249.

Concerning Pathology of Parkinsonism. M. Neustaedter and A. F. Liber. 264.

Paralysis following the Prophylactic Inoculation of Rabies Vaccine and Tetanus Antitoxin. F. G. Lindemulder. 284.

The Art and Practice of Psychiatric Examination. K. E. Appel. 292.

Youth is in the Saddle. F. J. Farnell. 312.

JOURNAL OF PHYSIOLOGY

Vol. 90. No. 2. July 1937.

The Secretory Response of the Posterior Pituitary to the Need for Water Conservation. A. Gilman and L. Goodman. 113.

Maintenance of Ovarian and Luteal Function in the Hypophysectomized Rabbit by Gonadotropic Hormones. J. M. Robson. 125.

Maintenance of Pregnancy and of the Luteal Function in the Hypophysectomized Rabbit. J. M. Robson. 145.

Distribution of Chloride in Frog's Skeletal Muscle immersed in Saline Solution. M. G. Eggleton, P. Eggleton, and A. M. Hamilton. 167.

Evidence for Electrical Transmission in Nerve. A. L. Hogkin:
Part I. 183.
Part II. 211.

Action Potentials Recorded from an Unstriated Muscle of Simple Structure. C. M. Fletcher. 233.

Vomiting produced, in the Cat, by Ligation of the Mesenteric Vein. K. J. Franklin and A. D. McLachlin. 254.

Vol. 90. No. 3. August 1937.

Liberation of Histamine from the Perfused Lung by Snake Venom. W. Feldberg and C. H. Kellaway. 257.

Liberation of Histamine from the Perfused Lung by Staphylococcal Toxin. W. Feldberg and E. V. Keogh. 280.

The Liberation of Histamine from the Perfused Lung by Peptone. W. Feldberg and W. J. O'Connor. 288.

A Study of Cholesterol in the Adrenal Gland in Different Phases of Reproduction in the Female Rat. D. H. Anderson and W. M. Sperry. 296.

Action of Adrenaline on the Serum Potassium. J. L. D'Silva. 303.

The Antistrychnine Action of Acetylcholine, Prostigmine, and Related Substances, and of the Central Vagus Stimulation. A. Schweitzer and S. Wright. 310.

The Behaviour of Crystallized Secretin when digested with Proteolytic Enzymes. G. Agren and E. Hammersten. 330.

The Aerobatic Metabolism of the Isolated Frog's Heart poisoned by Iodoacetic Acid. A. J. Clark, R. Gaddie, and C. P. Stewart. 335.

A Contribution to the Study of Ciliary Movement. A. E. Barclay, K. J. Franklin, and R. G. Macbeth. 347.

The Source in Blood of the Histamine-like Constituent. C. F. Code. 349.

The Reactivity during Œstrus and Pregnancy of the Rat Uterus to the Oxytocic Principle of the Posterior Pituitary Gland. J. B. Brooksby. 365.

Vol. 90. No. 4. September 1937.

The Female Prostatic Gland and Its Reaction to Male Sexual Compounds. V. Korenchevsky. 371.
The Action of Anticoagulants. J. O. Wakelin Barratt. 377.
The Rôle of Appetite in the Control of Body Weight. N. F. MacLagan. 385.
*Ascending Spinal Pathways of the Pupillo-dilator Fibres. A. A. Harper and B. A. McSwiney. 395
The Radiographic Examination of Dental Tissues in Relation to their Histological Structure. J. Thewlis. 403.
Excitation of the Action Potential of a Molluscan Unstriated Muscle. C. M. Fletcher. 415.
Some Characteristics of the Action of Urine upon Amphibian Melanophores. S. H. Raza and W. R. Spurrell. 429.
Maintenance of Œstrin of the Luteal Function in Hypophysectomized Rabbits. J. M. Robson. 435.
Oxidation of Glucose as Function of Its Supply. M. Wierzuchowski. 440.
The Behaviour of Muscle following Injection of Water into the Body. M. G. Eggleton. 465.
Reflexes from the Bladder and Large Intestine. A. E. Barclay and K. J. Franklin. 478.
The Rate of Excretion of Indian Ink injected into the Lungs. A. E. Barclay and K. J. Franklin. 482.
The Histamine-like Activity of White Blood Cells. C. F. Code. 485.
The Isolation of Histamine from the White Cell Layer of Centrifuged Rabbit Blood. C. F. Code and H. R. Ing. 501.

Ascending Spinal Pathways.—A study has been made of the pathway in the cord for the afferent impulses from the splanchnic region which bring about dilatation of the pupil. The authors were able to demonstrate that the pathway was through the posterior roots and then crossed within the segment to pass up the contralateral column. There was also a pathway lying in the ipsilateral column. (E. A. C.)

PHYSIOLOGICAL REVIEWS

Vol. 17. No. 3. July 1937.

The Rôle of Fat in the Diet. W. E. Anderson and H. H. Williams. 335.
Drugs affecting Parasympathetic Nerves. V. E. Henderson and M. H. Roepke. 373.
Physical Factors involved in the Activities of the Mammalian Kidney. F. R. Winton. 408.
Fatigue in Mental Work. A. G. Bills. 436.
Reversible Inactivations of Certain Hydrolytic Enzymes. L. Hellerman. 454.

Vol. 17. No. 4. October 1937.

Transmission of Nerve Endings by Acetylcholine. G. L. Brown. 485.
The Transmission of Sympathetic Nerve Impulses. A. Rosenblueth. 514.
Synaptic and Neuro-Muscular Transmission. J. C. Eccles. 538.
Cellular Changes in the Anterior Hypophysis with Special Reference to Its Secretory Activities. A. E. Severinghaus. 556.
Cellular Differentiation and Tissue Culture. W. Bloom. 589.
The Action of Morphine on the Digestive Tract. H. Krueger. 618.

PSYCHIATRIC QUARTERLY

Vol. 11. No. 3. July 1937.

Schizophrenic Thought. B. Pollack. 337.
Infant Feeding and Personality Disorders. J. Hill. 356.
Prognosis in Dementia Præcox. D. Whitehead. 383.
Psychiatric and Social Treatment. L. M. Hambrecht. 391.
The Mechanism of Continuous Bath Therapy in Excitement. G. M. Davidson. 424.
A Statistical Study of Benign Stupor in Five New York State Hospitals. H. L. Rachlin. 436.
A Note on the Rate of First Admissions with Traumatic Psychoses in New York State. B. Malzberg. 445.
Social Competence of the Feebleminded under Extra-Institutional Care. E. A. Doll and S. G. Longwell. 450.
Studies of Obsessive Ruminative Tension States. L. F. Woolley. 465.
Extramural Care in New York State. R. R. Steen. 481.
Technical Approaches used in the Study and Treatment of Emotional Problems in Children. J. L. Despert. 491.
Patients' Observations on Cure and Treatment. N. D. Black. 507.

Vol. 11. No. 4. October 1937.

The Position of the Occupational Therapist in a Plan of Research in Schizophrenia. N. D. C. Lewis. 537.
*Psychiatric Implications in Occupational Therapy. L. E. Hinsie. 554.
Dementia Præcox ; Preventable. P. Milici. 552.
*Intracranial Neoplasms ; Their Incidence and Mental Manifestations. J. L. Hoffman. 561.
Streptococcic Meningitis with Recovery in a Case of General Paresis. I. M. Derby and M. Zeifert, 576.
Epileptic Psychosis ; A Clinical Study. I. Schnap. 582.
The Psychology of the Headache ; a Case Studied Experimentally. Jule Eisenbud. 592.
Racial Variation in the Blood-Cerebrospinal Fluid Barrier of Normal Children. F. A. Meltler, M. Robinow, H. G. Stelling, C. Mc. K. Burpee, and M. K. Amdur. 620.
Objective Signs of Invalidity of Stamford-Binet. Tests. Z. A. Piotowski. 623.
Report on Tuberculosis Survey Recently Complete

at Marcy State Hospitals. D. A. Harrison and G. Schein. 637.
Fire Prevention in State Hospitals. C. W. Hutchings. 643.
Studies in Obsessive Ruminative Tension States. L. F. Woolley. 654.
Technical Approaches used in the Study and Treatment of Emotional Problems in Children. Part V. J. Louise Despert. 677.

Psychiatric Implications in Occupational Therapy.—The aim of the occupational therapist is to promote and encourage mature physical and mental reactions. When a patient is removed to a mental hospital the change is very abrupt and his emotions are detached from his home surroundings. It is the business of the occupational therapist to help these patients to create new interests or to assist in the growth of the individual. The therapist represents the head of the family and as such he should use his relationship with the patients in the furtherance of progressive measures. Concerning treatment from the standpoint of diagnosis it is suggested that the patients be divided into three large groups. The first group consists of patients whose illness is a consequence of definite organic disease or inadequacy. With this type the author finds it is sufficient to make the natural environment available to them. The second group consists of psychoneurotics who require least of the occupationist's attention, as there is nothing much to be gained from forcing them to do things against their will. The third group comprises the psychotics who seem to benefit considerably under the facilities of occupational therapy. Regarding the facilities, the arts and crafts and athletics are found to be most beneficial, and for the more advanced grade social entertainments, teas, cards, dramatics, etc., are provided.

Intracranial Neoplasms : Their Incidence and Mental Manifestations.—This survey is based on 2,000 consecutive post-mortem examinations performed on mental patients who died at St. Elizabeth's Hospital in the period from 1923 to 1935. In only 19 cases was permission refused for examination of the brain. The number of tumours encountered in the series was 69 ; an incidence of 3·45 per cent. Of the 69 brain tumours, 51 were primary growths and 18 were carcinomatous metastases. Of the primary tumours 34 were meningiomata. Many of these were accidental post-mortem findings having given no hint of their existence during life. Twenty-eight of these tumours were less than 2·0 cm. in diameter. The remainder of the group consisted of 13 gliomata, four pituitary tumours (adenocarcinoma), and two tumours of the cranial nerves. Of the meningiomata exactly half were located in the frontal area, four in the temporal, six were in the cerebellar or cerebellarpontine, two were occipital, and one parietal. In five instances there were multiple growths. The author confirms the universally accepted view that there is no psychosis characteristic of the cerebral tumour.

REVUE NEUROLOGIQUE

Vol. 68. No. 1. July 1937.

Physiologie et Pathologie Générale de la Douleur. (Physiology and general pathology of pain.) A. Baudouin and H. Schaeffer. 15.
La Physiopathologie de la Douleur d'Origine Centrale. (The physiopathology of pain of central origin.) G. Riddoch and M. Critchley. 77.
La Douleur dans les Affections Organiques du Système Nerveux Central (Partie Anatomo-Clinique). (Pain in organic diseases of the central nervous system.) R. Garcin. 105.
La Douleur dans les Maladies Organiques du Système Nerveux : Nerfs Périphériques. (Pain in organic diseases of the nervous system : Peripheral nerves.) J. Dechaume. 174.
Douleur Sympathique et Douleur Viscérale. (Sympathetic and visceral pain.) Ayala. 222.
La Douleur Vue par un Psychiatre. (A psychiatrist's view of pain.) N. Peron. 921.
Diagnostic de la Réalité de la Douleur. Considérations Médico-Légales. (Diagnostics of the reality of pain. Medico-legal considerations.) O. Crouzon and H. Desoille. 248.
Neurochirurgie de la Douleur. (The neuro-surgery of pain.) R. Leriche. 317.
La Roentgenthérapie de la Douleur. (X-ray treatment of pain.) J. Haguenau and L. Gally. 359.

A number of papers on the physiology and pathology of pain in organic nervous disease, visceral pain, pain in psychiatric disorders, and the surgical- and radiotherapy of pain. (D. D.-B.)

Vol. 68. No. 2. August 1937.

*Les Chiens sans Moelle du Professeur Hermann. (Professor Hermann's dogs in which the spinal cord had been excised.) J. Dechaume. 409.
*La Phénomène du Genou dans la Claudication Intermittente. (The knee phenomenon in intermittent claudication.) D. Pantchenko. 436.

Effect of Removal of Spinal Cord.—Excision of the spinal cord up to the D1 segment in the dog, with six survivals from 50 to 418 days. With remarks on the general aspects of control of nutrition, vascular tone, and control of blood sugar and temperature. (D. D.-B.)

Intermittent Claudication.—Sitting or lying with the legs crossed so that one knee compresses the popliteal space of the other limb brings about pains in the calf in this condition. (D. D.-B.)

Vol. 68. No. 3. September 1937.

Les Méningiomes Olfactifs. (Olfactory meningiomas.) M. David and H. Askenasy. 489.

Olfactory Meningiomas.—A clinical and anatomical analysis based on a series of 26 cases from the Neurological Service of the Hôpital de la Pitié, from a total of 195 of operated meningioma. From this series of cases 76 were of meningioma of the convexity, 46 sphenoidal, and 21 from the tuberculum sellæ. (D. D.-B.)

RIVISTA DI NEUROLOGIA, NAPOLI

Vol. 10. Part 3. June 1937.

*Studio del Ricambio Idro-Salino in un Caso d'Isterismo. (Study of the Water-Saline Exchange in a Case of Hysteria.) C. Pero. 257.

*Sopra due Casi di Parkinsonismo Encefalitico della Forma Tardivissima (Considerazioni Etio-Patagenetiche). (Two cases of encephalitic Parkinsonism of very slow development.) F. Vizioli. 276.

*Spasmo Funzionale Isolato dei Pellicciai del Collo. (An isolated functional spasm of the platysma.) R. Cristini. 285.

Un Nuovo Metodo di Impregnazione Argentica dell'Oligodendroglia. (A new method of silver staining of the oligodendroglia.) V. Della Pietra. 295.

*Glioblastoma del Lobo Temporale Destro. (A glioblastoma of the right temporal lobe.) F. Giardini and R. Giorgini. 304.

Study of Water-saline Exchange in Hysteria.—This case exhibited manifestations of severe hyperkinesis. An accurate estimation was kept of the diuresis as well as of certain ions which influence the water exchange both during remissions and in the periods of agitation. From his observations the author concludes that the diencephalon and posterior pituitary have a most important influence on the symptoms met with. This conforms with the theory of those authors who believe that hysteria is a syndrome due to dysfunction of the nuclei of the diencephalon. (R. G. G.)

Two Cases of Encephalitic Parkinsonism.—These two cases were typical, with a well-documented history of epidemic encephalitis several years previously. The first was precipitated by a cranial injury and the second by an accidental carbon monoxide intoxication. The author discusses how far the development of the syndrome was due to these accidents and how far to a recrudescence of the encephalitis. He concludes that they should be regarded as fundamentally due to the encephalitis and therefore placed in the category of late and discontinuous manifestations of this disease. (R. G. G.)

Isolated Spasm of the Platysma.—A rare condition only occasionally mentioned in the literature and probably of emotional origin. (R. G. G.)

Glioblastoma of Temporal Lobe.—This case died somewhat suddenly as a result of a hæmorrhage into a tumour in the right temporal lobe which had run a long course with very few symptoms. (R. G. G.)

Vol. 10. No. 4. August 1937.

*Contributo alla Diagnosi dei Tumori del Lobo Parietale con Particolare Riguardo all'Atrofia Muscolare di Origine Cerebrale. (Contribution to the diagnosis of tumours of the parietal lobe with particular regard to muscular atrophy of cerebral origin.) O. Fragnito. 345.

*Respirazione e Catatonia. (Respirations and catatonia—experimental variations.) M. de Mennato and M. d'Arrigo. 357.

*Sulla Permeabilità della Barriera Emato-Liquorale nelle Intossicazioni Sperimentali da Cantaridina e da Mercurio. (On the permeability of the blood-fluid barrier in experimental intoxication with cantharides and mercury.) G. Renzetti. 373.

*Le Sindromi Neuro-Anemiche. (The Syndrome of Anæmia.) P. Coppola. 385.

Contribution to the Diagnosis of Tumours of the Parietal Lobe.—A case is described and the author quotes others described in the literature. He discusses the causation, which must presumably be due to vasomotor disturbances. These atrophic changes are more liable to occur when the right parietal lobe is affected than when the left is the seat of the lesion, when of course aphasia is apt to develop. The author is not convinced by the theory that one side of the brain is concerned with the higher function of speech while the other deals with "lower" functions, such as vasomotor control, etc., since if this were so the muscular atrophy would be seen all over the body and not localized to one side. (R. G. G.)

Respirations and Catatonia.—In catatonia there is a diminution of the amplitude of the respirations and a compensatory increase of rate. This diminution of amplitude would seem to be due to the hypertonicity of the muscles since the increase in rate shows that the respiratory centres are active. In melancholia, on the other hand, in which the muscles are relaxed the respirations are normal sometimes with an increase in amplitude. (R. G. G.)

Permeability of the Blood-fluid Barrier.—Certain poisons cause the same sort of lesions in the choroid plexus as they do in the kidney. These morphological lesions are not, however, accompanied by alterations of the quotient of permeability to bromine

or by alterations in the fluid. The theory which would seek to show that the cerebrospinal fluid is produced in the same way as the urine is not, therefore, upheld and still lacks experimental proof. (R. G. G.)

Anæmia and Nervous System.—Three forms are mentioned: Lichtheim's syndrome (sub-acute combined degeneration); polyneuritis with anæmia; cerebral lesions and symptoms with anæmia. (R. G. G.)

Vol. 10. No. 5. October 1937.

*Sull'Origine delle Fibre Muschiose del Cervelletto. (On the origin of the moss fibres of the cerebellum.) L. Rosiello. 437.

*Tumore del Lobo Parietale Sinistro con Amiotrofia Controlaterale. (Tumours of the left parietal lobe with contralateral muscular atrophy.) R. Cristini. 456.

*Reazioni Citologiche del Liquor nella "Riattivazione" con Sali di Bismuto. (Cytological reactions of the cerebrospinal fluid to bismuth salts.) L. Ponzoni. 476.

*Sindromi Neurologiche da Ernia del Nucleo Polposo. (The neurological syndrome of hernia of the nucleus pulposus.) A. Rubino. 491.

Moss Fibres of the Cerebellum.—The author finds that the hemisection of the spinal medulla results, in the dog, in degenerative alterations of the moss fibres of the superior vermis of the cerebellum, while the climbing fibres remain intact. The moss fibres then represent the termination of the spinocerebellar tracts while the climbing fibres seem to have a different origin. (R. G. G.)

Tumours of Parietal Lobe with Muscular Atrophy.—A case of left parietal tumour is described in which in addition to other symptoms marked muscular wasting of the limbs on the right side was found. The localizing importance of this sign is pointed out. (R. G. G.)

Cytological Reactions in the Cerebrospinal Fluid.—Injections of bismuth salts both in syphilitic and non-syphilitic subjects were carried out, but no substantial and significant differences in the cytological reactions between the two groups were noted. (R. G. G.)

Syndrome of Herniation of the Nucleus Pulposus.—A case is described which was diagnosed on the clinical signs and on repeated radiological confirmations. The symptoms are localized lumbar pain and impairment of movement of the lumbar vertebræ. Root pains may also be experienced. The nucleus may be herniated into the vertebral body or into the spinal canal, and the pathogenesis and clinical features of both these forms are fully discussed. (R. G. G.)

RIVISTA DI PATALOGIA NERVOSA E MENTALE

Vol. 49. No. 3. May 1937.

*Contributi di Neuro-Chirurgia. (Neuro-surgical contributions.) S. D'Este and P. Varenna. 467.

Neuro-Surgical Contributions.—This is a study of a second group of cases supplementary to those described by the authors in the *Rivista* of 1933, pp. 474–90. The present account relates to cases of Raynaud's disease and allied conditions and occupies 200 pages. It therefore cannot be adequately abstracted. The clinical and pathological features of eight cases of Raynaud's disease and nine cases of spontaneous gangrene (endarteritis obliterans) are described in detail, and the nature of the conditions and lines of treatment are fully discussed. One particularly interesting case is described of an associated form where in the same hand there occurred Raynaud's disease, Weir-Mitchell's syndrome, and spontaneous gangrene. The technique is described of periarterial section and perineural section along with nerve stretching and fasciotomy, and the classification and nomenclature of diseases of the blood vessels is criticized. This essay is profusely illustrated and amply documented. (R. G. G.)

Vol. 50. No. 1. July 1937.

*Malattia di Lindau e Malformazioni Encefaliche. (Lindau's disease and cerebral malformation.) V. Porta. 1.

*Sulla Stimolazione Galvanica delle Singole Parti del Labirinto Acustico. (On galvanic stimulation of single parts of the acoustic labyrinth.) P. Tullio and L. di Bella. 36.

*Sui Quadri Isto-Patologici della Oligodendroglia Cerebrale Umana. (On the histopathological picture of the oligodendroglia of the human brain.) F. Cardona. 48.

Sul Istopatalogia Cerebrale del Alcoolismo Cronico. (On the cerebral histopathology of chronic alcoholism.) F. Cardona. 63.

*La Remissione della Sintomatologia Demenziale Negli Encefalitici Sottoposti Alla Cura Bulgara. (The remission of symptoms of dementia under the "Bulgara" treatment. Alcoholic decoction of the root of atropa Belladonna Bulgara.) C. Meco. 75.

*Studio sul Comportamento del "Fenomeno d'Ostacolo" di Donaggio: Contributo alle Richerche sulla Terapia Malarica e Piretogena. (Studies on the behaviour of the phenomenon of "Ostacolo of Donaggio"; prevention of precipitation of a colouring matter in the cerebrospinal fluid with ammonium molybdate. A contribution to malarial and pyrogenic therapy.) G. Giorgi. 96.

*Isterismo ed Encefalite Epidemica Cronica (Considerazioni su di un Caso Clinico). (Hysteria and chronic epidemic encephalitis.) F. Cardona. 134.
*Sui Quadri Istopatologici della Microglia Cerebrale Umana. (On the histopathological picture of the neuroglia in the human brain.) F. Cardona. 141.
*Sulle Neuro-Discrinie Diencefalo-Tiroidee. (On a case of neuro-endocrine dysfunction affecting the diencephalon and thyroid apparatus.) G. Patressi. 148.

Lindau's Disease and Cerebral Malformation.—A case of probably familial reticular-angioblastoma of the cerebellum in a child of three years is described. This was accompanied by multiple extensive and serious malformations of the cerebrum all referable to a disturbance occurring at the same period of embryological development. The author discusses the importance of tracing to their genesis the malformations in Lindau's disease and their affinity with other malformations in the course of development of the central nervous system and of the internal organs. (R. G. G.)

Galvanic Stimulation of the Acoustic Labyrinth.—The galvanic current applied with two poles to the membranous semicircular canals in a pigeon provoked a movement in the canal stimulated opposite to the direction of the current. With unipolar stimulation a movement is produced which corresponds to that produced by a rhythmic stimulus of a faradic current or of sound. Applying the electrodes to the auditory meatus and paralysing (an ampulla) with cocaine movements are obtained in the other canals by the extension of the excitation to the whole of the labyrinth. (R. G. G.)

Oligodendroglia of the Human Brain.—Studying the oligodendroglia in the human brain in various pathological conditions the author analyses especially the importance of the methods and of the interpretation of results. Finally he describes the pictures which the current methods of silver staining present in the study of the oligodendroglia and discusses their significance. (R. G. G.)

Cerebral Histopathology of Chronic Alcoholism.—Modern methods of examination (especially directed to the diencephalon) seem to show no localized histopathological pictures in Korsakoff's syndrome or in delirium tremens. (R. G. G.)

Remission of Symptoms under the "Bulgara" Treatment.—Cases of encephalitic Parkinsonianism complicated by dementia were treated by "bulgara" and the results noted. More or less improvement resulted, especially in the symptoms of dementia. Often the remission of the demented state was accompanied by excitement, but it is desirable if we are to understand the action of "bulgara" to study its use in other forms of mental disease. The author thinks that it acts by removing an inhibition and that both the bradykinesia and the apparent dementia are due more to an inhibitory action than to true degenerative processes. (R. G. G.)

Behaviour of the Phenomenon of "Ostacolo of Donaggio."—After reviewing this reaction in various physiological and pathological conditions the author investigated the changes consequent upon malarial and hyperthermal treatment. The reaction is positive from the beginning of malarial therapy and lasts for some days after the fever subsides. The significance of these reactions and those found in other forms of hyperthermal therapy are discussed, but no very definite conclusions can yet be formulated. (R. G. G.)

Hysteria and Chronic Epidemic Encephalitis.—A description of a case showing chronic epidemic encephalitis, major hysteria, and Parkinsonianism and a discussion of the dependence of all these conditions on the function of the extrapyramidal system. (R. G. G.)

Neuroglia in the Human Brain.—A discussion of the general appearance of the microglia and their significance in the diagnosis of various pathological conditions. (R. G. G.)

Neuro-Endocrine Dysfunction.—A young man after a severe mental shock became asthenic and put on fat without disturbance in the genital functions. At the same time he showed signs of diffuse changes of the skin of the type of adult scleroderma of Buschke and of Acanthosis nigricans. There was an increase of neutral fats in the serum, a reduction of basal metabolism, and a hypoglycæmia. Treatment by thyroxin produced favourable results. The pathology of hyperlipæmia, scleroderma, and acanthosis are fully discussed. (R. G. G.)

Vol. 50. No. 2. September 1937.

*Per Una Migliore Conoscenza della Istoarchitettonica della Regione Giganto-Piramidale Umana. (Towards a better knowledge of the histological architecture of the large pyramidal cell region in the human brain.) V. Tronconi. 225.
Associazione di Meningiomi Multipli e di "Pachimeningite Emorragica Interna." Considerazioni sulla Istogenesi dei Due Processi Morbosi. (Association of multiple meningiomata and of internal hæmorrhagic pachimeningitis.) A. Pacifico. 299.
Sopra una Particolare Sincinesia Nell-Uomo. Studio della Sincinesia a Proposito di un Caso Clinico di Tumore del Midollo Cervicale. (On a special synkinesis in man.) O. Meco. 326.
*Contributo alla Delimitazione Clinica della Anoressia Mentale. (A contribution to the clinical delimitation of psychic anorrhexia.) P. Ottonello. 353.
*Su di una Particolare Alterazione della Motilità Oculare in Soggetto con Torcicollo Spasmodico. (On a special alteration of the movement of the eyes in a subject with spasmodic torticollis.) E. Leisch. 386.
*Sulla Presenza di Cellule Gangliari nel Tronco del

Simpatico Cervicale dell'Uomo. (On the presence of ganglion cells in the sympathetic trunk in man.) L. Eletto. 401.

*Sulle Alterazioni Mieliniche da Cianuro. (On the alterations in the myeline sheaths under the influence of cyanide.) G. Jervis. 410.

Architecture of the Large Pyramidal Cell Region.—After discussing the value of localization of lesions in particular areas or layers of the pyramidal area in brains which have been examined because the patient died of some nervous disease, the author points out that if brains are examined taken from patients dying of diseases which have nothing to do with the nervous system, a cerebral reaction may be discovered which is the same as that described in many diseases of that system. It is therefore very necessary to recognize this before a histopathological picture of any given nervous disease is formulated. (R. G. G.)

Psychic Anorrhexia.—The author describes three cases and discusses the question of ovarian function in these conditions. He suggests that psychotherapy is not so successful as is sometimes made out, and brings forward some arguments in favour of physiopathological mechanisms in these conditions. (R. G. G.)

Movement of the Eyes in a Spasmodic Torticollis.—The case was probably one of epidemic encephalitis. The abnormal phenomenon was an impossibility to move the right eye in turning the eyes to the right without jerking, while it should move evenly with the other. This was not due to uneven impulses from the cervical nuclei, since this was excluded. (R. G. G.)

Presence of Ganglion Cells in Sympathetic Trunk.—Microphotographs are given which show such cells, and they are assumed to be residues of the primitive neural cells from which the fibres are derived. (R. G. G.)

Alterations in Myeline.—The following experimental factors are discussed: the difference in the total maximal doses which produce demyelinization; the differences of single maximal doses necessary for this process; the time required for the summation of separate doses; and finally the maximal dose which can be reached before the death of the animal. (R. G. G.)

SCHWEIZER ARCHIV FÜR NEUROLOGIE UND PSYCHIATRIE

Vol. 38. No. 2. 1937.

*Beitrage zur postembryonalen Entwicklung der Kleinhirnrinde beim Menschen. (Contributions to the post-embryonic development of the cerebella cortex in man.) M. L. Borowsky. 225.

*Studien zur Frage der symmetrischen Gefässreaktionen im Gehirn. (The question of symmetrical vascular reactions in the brain.) C. Boukis and H. Hoff. 240.

Über das Adie'sche Syndrom. (Adie's syndrome.) M. Dressler and H. Wagner. 246.

Vergleichend-anatomische Untersuchungen über die basale optische Wurzel, die Commissura transversa Gudden und über eine Verbindung der Netzhaut mit dem vegetativen Gebiet im Hypothalamus durch eine "dorsale hypothalamische Wurzel" des nervus opticus bei Amnioten. (Comparative anatomy of the basal optic root, the transverse commissure of Gudden, and a connection of the retina with the vegetative hypothalamic area through a "dorsal hypothalamic root" of the optic nerve in amniotes.) E. Frey. 255.

Die Vererbung der Schizophrenie. (Heredity in schizophrenia.) A. Galatschjan. 291.

*Familienkundliche, körperliche und psychopathologische Untersuchungen über eine Friedreich-Familie. (Genealogical, physical, and psychopathological investigations of a family with Friedreich's disease.) D. Klein. 320.

Über Akalkulie. (Acacalculia.) E. Krapf. 330.

*Über die Schizophrenie im Kindesalter. (Schizophrenia in childhood.) J. Lutz. 335.

Zwei Fälle von Kindstötung in psychiatrischer Beurteilung. (Psychiatric comment on two cases of infanticide.) M. Pfister-Ammende. 373.

*Veränderungen des Zentralnervensystems bei Vergiftungen durch Schlafmittel (Barbitursauregiftungen). (Changes in the central nervous system in barbiturate poisoning.) S. Scheidegger. 388.

Development of the Cerebellar Cortex in Man.—The cerebellar glia and the Purkinje cells are derived entirely from the internal embryonic layer. The Purkinje cells are still immature at the time of birth and normally the migration of Purkinje cells and Golgi cells from the ventricular matrix through the white matter to the cortex still continues in extra-uterine life. The Golgi cells, however, are morphologically mature at the time of birth. The development of the cerebellar cortex is essentially complete after the first year of life. (K. S.)

Vascular Reactions in the Brain.—In the dog's brain an artery was directly stimulated by light mechanical, thermal, and chemical stimuli, causing a short transient constriction and following a longer dilatation. In the areas of the anterior and middle cerebral artery there was no accompanying response of the corresponding artery on the contralateral side. After stimulation of a "certain vessel" in the area of the posterior cerebral artery the corresponding vessel of the opposite hemisphere showed the same response as the stimulated vessel. (K. S.)

Family with Friedreich's Disease.—Continuation and conclusion of a paper which was previously reported. (K. S.)

Schizophrenia in Childhood.—A survey of the literature and a description of the author's own cases are given. There are two forms of psychoses in children which the author regards as infantile schizophrenia. (K. S.)

Central Nervous System in Barbiturate Poisoning.—Thirteen cases were examined. The vessels show fatty degeneration, sometimes ring hæmorrhages and perivascular hæmorrhages. In some instances areas of "palling" of the cortex are to be seen. The glia undergoes both proliferative and regressive changes. The glia proliferation is sometimes in relation to vessels. The chief changes are seen in the thalamus, the globus pallidus, the cerebral cortex, and the cerebellum. (K. S.)

ZEITSCHRIFT FÜR DIE GESAMTE NEUROLOGIE UND PSYCHIATRIE

Vol. 159. No. 2. July 1937.

Die physikalischen Methoden der Liquordiagnostic. (Physical methods in examination of cerebrospinal fluid.) F. Roeder. 163.
*Beiträge zur Lehre von der Seelenblinheit. (Contributions to the study of optic agnosia.)

Study of Optic Agnosia.—In these papers two cases are described showing optic agnosia as one of the symptoms. Both had extensive softenings involving the left occipital region and extending forward, with secondary degenerations in the corpus callosum and the white matter of the right side. Two other cases are described without optic agnosia, with softenings of the left occipital lobe, but without the secondary degenerations of the other side. The disturbance of association fibre tracts is functional rather than anatomical in nature. The left hemisphere with its association fibres is cut out, and its function taken over by the right hemisphere, which lacks associative experience, so there is considerable resistance or delay in association functions. There is a full discussion of the views of others. (G. M. G.)

Vol. 159. No. 3. August 1937

Zur actionsstromanalys der Sehnenreflexe beim Pallidum-Nigrasyndrom. (The analysis of action currents in tendon reflexes in the syndrome of the globus pallidus and substantia nigra.) R. Deschla. 345.
Erfahrung über Morphinismus, und Behandlung von Morphinisten in einer Privatanstalt. (The study of morphinism, and the treatment of morphinists in a private institution.) H. Schaller. 349.
Über eine optisch-agnostische Störung des "Physiognomie-Gedächtnisses." (An optic-agnostic disturbance of memory for faces.) H. Hoff and O. Pötzl. 366.
*Vegetative Störungen in Rotenkern-Thalamussyndrom. (Vegetative disturbances in the syndrome of the thalamus and red nucleus.) A. Széky. 396.
Über eine neue Untersuchungsmethode des Hornhaut und Bindehaut-reflexes. (A new method of studying corneal and conjunctival reflexes.) V. Cavka. 405.
Selbstbeobachtungen im hypoglykämischen Zustand. (Self-observations on the hypoglycæmic state.) J. Wiedeking. 417.
Delirium Tremens und Alkoholhalluzinose im Rorschachschen Formdeutversuch. (The Rorschach test in delirium tremens and alcoholic hallucinosis. A. Weber. 446.

Vegetative Disturbances of the Thalamus and Red Nucleus.—A girl of 16 with unilateral motor symptoms of a cerebellar type, intention tremor, sensory disturbances, especially thermal, and choreo-athetosis. She also showed vasomotor instability and increased perspiration on the affected side. The vegetative functions of the hypothalamus are discussed in relation to its connections with the thalamus. (G. M. G.)

Vol. 159. No. 4. September 1937.

*Erbanlage und Epilepsie. IV. Ergebnisse einer Nachkommenschaftsuntersuchungsn epileptikern (zum empirischen erbprognose der Epilepsie). (Heredity and epilepsy. IV. Results of an investigation of the descendants of epileptics.) K. Conrad. 521.
Ergebnisse und bemerkungen zur frage des durch Cardiazol kunstlich hervorgerufen epileptiformen anfalles. (Observations on the question of epileptiform attacks artificially produced by Cardiazol.) B. Wichmann. 582.
Zur empirischen Erbprognose der Psychopathie. (Untersuchungen an Kindern von Psychopathen.) (The empirical heredity-prognosis in psychopathy.) H. Riedel. 596.
Über "Mischpsychosen." (On mixed psychoses.) J. Wyrsch. 668.
*Zur Frage der Toxizität des Liquor cerebrospinalis. (The toxicity of the cerebrospinal fluid.) K. F. Scheid. 694.
*Zur Frage der biologischen Wirksamkeit des Schizophrenliquors. (The biological activity of the cerebrospinal fluid of schizophrenics.) E. Gamper and A. Kral. 697.
Ergebnisse der Insulinshockbehandlung bei Schizophrenie. (Results of the treatment of schizophrenia by insulin shock.) M. Marzyński and S. Witek. 704.
Der "defectgeheiltle Paralytiker" (Pönitz) als sozialpsychiatrisches Problem. Dargestellt auf Grund eigener Untersuchungen in den schlesischen Heil-uns Pflegeanstalten. (The social-psychiatric problem of the paretic with residual defect: from investigations in the medical and nursing institutions of Schleswig.) K. H. Parnitzke. 723.
Die Stellung des Kindes im Wahnsystem der Mutter. (The place of the child in the delusion system of the mother.) B. Bärtschi-Rochaix. 746.
Über den Einfluss hypnotischer Erregungszustände auf des Gasaustausch. (The influence on gaseous exchange of disturbances under hypnosis.) E. Fulde. 761.
Eine experimentalle Untersuchung zur Frage der kriminellen hypnotisch-suggestiven Breinflussbarkeit. (An experiment in criminal hypnotic suggestion.) J. Haupt. 767.
Hemiatrophia faciei. Hypertrophia cruciata duplex. E. Henssge. 769.
Klinischer und histopathologischer Beitrag zur hereditären spastischen Spinalparalyse. (Clinical and histopathological studies on hereditary spastic spinal paralysis.) A. Kahlstorf. 774.
Klinisch-anatomischer Beitrag zur Kenntnis der Chorea minor. (Clinical and anatomical contribution to the study of chorea minor.) G. G. Noto. 781.

Heredity and Epilepsy.—A statistical study of 2,600 children of epileptic parents showed that 655 died in early childhood. Of the rest 6–9 per cent. were epileptic, 6·5 per cent. feebleminded. When other mental and somatic deficiencies were considered, about 50½ of the children appeared to be undesirable from the heredity aspect. The figures were much larger in the group

of idiopathic epilepsy than among the symptomatic group. (G. M. G.)

Toxicity of the C.S.F.—This paper gives details of 51 experimental subcutaneous injections of cerebrospinal fluid into young mice. Schizophrenic and other fluids were used. During a period of four weeks all the mice died from an intercurrent epidemic. Apart from that one mouse died of intestinal disease, and only one mouse died as a result of the injection. Concentration and adsorption of the "toxic principle" was tried, but gave negative results. The findings of Gamper and Kral were not confirmed. (G. M. G.)

Biological Activity of the C.S.F.—The toxicity of the cerebrospinal fluid of schizophrenics was compared with that of other nervous and mental diseases by the subcutaneous injection of fresh cerebrospinal fluid into young mice. Of 43 non-progressive psychoses two gave a positive result (at least one mouse died in three weeks). Of 78 cases of organic disease of the C.N.S., 31 were positive, 17·5 per cent. of the mice dying, while of 103 schizophrenics there were 53 positive, while 23 per cent. of the mice died. Acute cases were more toxic than chronic ones. Dialysis of schizophrenic C.S.F. was tried and the toxic substance found to be dialysable. The toxic substance was found in two out of nine ether extracts. Concentration of the fluid makes it more toxic. (G. M. G.)

ZENTRALBLATT FÜR NEUROCHIRURGIE

Vol. 2. Nos. 5 and 6. August and September 1937.

*Subchiasmal Aneurysm treated by Implantation of Muscle. A. A. McConnell. 269.
*Eine neue Operations-methode bei Trigeminusneuralgie. Durchscheidung des Tractus spinalis trigemini. (A new operation for trigeminal neuralgia: cutting the Tractus spinalis.) O. Sjöquist. 274.
Zur Frage der extraventrikulären Ependymome. (Extraventricular ependymoma.) A. Giampalmo. 281.
Zur Technick der Arteriographie. (On the technique of artiography.) M. Zehnder. 283.
*Ein Beitrag zur Klinik der Frontaltumoren. (A contribution to the symptomatology of frontal tumours.) A. Torkildsen. 291.
*Über intrakranielle Epidermoide. (Intracranial epidermoids.) L. Findeisen and W. Tönnis. 301.
*Das Oligodendrocytom der Sehnervenkreuzung. (Oligodendrocytoma of the decussation of the optic nerve.) E. Busch and E. Christiansen. 315.
Über eine isolierte Störung nach Olnarischädigung. (An isolated disturbance following lesion of the ulnar nerve.) K. Horsch. 320.
Solitäres Neurinomder Mundhöhle. (Single neurinoma of the oral cavity.) G. Jorns. 325.
*Hirndrück — Hirnösen — Hirschwellung. (Intracranial pressure and cerebral œdema.) G. Häussler. 328.
*Die subduralen Hämatome. (Subdural hæmatoma.) M. Zehnder. 339.

Subchiasmal Aneurysm.—A male aged 34 had a spontaneous subarachnoid hæmorrhage and was very ill with a right-sided flaccid hemiplegia and incontinence. Recovery in six weeks. Four months later bilateral central scotomata were found. X-ray of sella and encephalography negative. Operation, a dark, rounded tumour was seen just below the chiasma, not pulsating. Well opened and muscle graft thrust in; held in place for 15 minutes. Headache disappeared, complete recovery of vision 9 months later. (G. J.)

Method of Operation for Trigeminal Neuralgia.—In this very interesting paper the author describes a new operation for trigeminal pain. It consists in the making of a small incision in the side of the medulla oblongata immediately below the exit of the lowest of the filaments of the vagal root. This incision should be 3–4 mm. long and 3–3·5 mm. deep. Deeper than 3·5 mm. there is a risk of wounding Nucleus ambiguans. Sjöquist by this section divides the descending root of trigeminus and gets analgesia without anæsthesia in the first, second, and part of the third division. The analgesia was always most dense in the area supplied by the ophthalmic division and least in the mandibular region. He has carried out this operation four times without ill-effect, save that in one there was a lasting unilateral vagal paresis. One of his cases was a post-herpetic neuralgia, two had severe paræsthesias following subtotal resection of the trigeminal root in the middle fossa (in one the stellate ganglion had been already removed without relief), one was a frank tic doloreux. The only one permanently relieved was the last, the first case of neuralgia cured by this method. The operation is simple, but it is interesting to observe that the deep, boring, pulling, burning pains of herpetic neuralgia, of atypical neuralgia, and of post-operative anæsthesia dolorosa cannot be improved by nerve section proximal to the nucleus. The paper is illustrated by excellent photographs of the patients, showing the analgesic areas, but the diagrams of the actual section might have been clearer. (G. J.)

Symptomatology of Frontal Tumours.—An analysis is made of 31 frontal tumours from the material of the Oslo clinic between the years 1920–1935, 154 verified cases. Considerable attention is paid to "frontal ataxia" and the author discusses the various theories for its development (crowding of the hemispheres on to the cerebellum, interference with the fronto-pontine-cerebellar fibres). He describes a case in which a subtentorial exploration was made for a right frontal glioma. He finds headache and epileptic fits to be the earliest signs, whilst visual disturbances are late,

though then common. Epilepsy is commoner with the gliomas than with the meningiomas. Increase in the albumen and globulin in the cerebrospinal fluid was found in some of the gliomas as well as the meningiomas. The significance of these findings is not discussed. (G. J.)

Intracranial Epidermoids.—The authors state that about 200 cases of intracranial epidermoids are recorded in the literature, of which 66 were operated upon. They report 13 new cases: six in the cerebellopontine angle, two at the chiasma, one in the fissure of Sylvius, three in the lateral ventricle, one in the quadrigeminal region. In a very well illustrated article the cases are described. The first example was found by chance during a posterior fossa approach to the sensory root to relieve the patient of what was thought to be an uncomplicated neuralgia. Examples are shown of the characteristic spotted or flecked appearance of the cholesteatoma in the ventriculograms. Seven of the cases are back at work; there were three post-operative deaths. (G. J.)

Oligodendrocytoma of the Optic Nerve.—A case of glioma of the optic nerve in a child with neurofibromatosis is described. There were bilateral optic atrophy, bilateral enlargement of the optic foremina, deepening of the sulcus chiasmatis. It is concluded that the diagnosis with the foregoing findings will always be oligodendrocytoma. (G. J.)

Cerebral Œdema.—This is an extremely comprehensive and interesting review, which will be profitably consulted by all those interested in œdema of the brain. There are 300 references. (G. J.)

Subdural Hæmatoma.—An extensive study of this always interesting subject is made. The author admits that the pathogenesis is not always clear in every respect, although trauma admittedly plays the most important part. It is surprising how slight the trauma may be. In this case there was a hit on the cheek; heading a football or a blow in boxing may lead to a fatal subdural bleeding. Generally the author thinks the source of the bleeding is parasagittal and the blow most commonly occipital. He believes that there are three factors in determining the general pathology of the clot: on the one hand the mass of the effused blood, on the other the resorption possibilities and the organizing power of the dura. With small quantities of blood a pachymeningitis tends to be produced; only the smallest quantities can be entirely resorbed. Although there are no lymphatics in the dura, there are thin-walled "lymphatic-like" veins and endothelial-lined spaces. It is not yet known how far these may be concerned in absorption. Further, he accepts Gardner's explanation of osmosis as the cause of the increase in size of the hæmatoma. He suggests that Schörcher's theory of homolateral pupillary dilatation by stimulation of the sympathetic is correct, and mentions a case of fracture of the skull, with facial palsy, in which pallor of the face and neck was present together with the Hutchinsonian pupil. He advocates the four-point drill-hole method of Fleming and Jones as the best method of treatment. There is a reproduction of an admirable angiogram typical of a subdural hæmatoma. (G. J.)

BOOK REVIEWS

THE BIOLOGY OF HUMAN CONFLICT

Trigant Burrow

(Macmillan & Co., Ltd., New York. 1937. 15*s*.)

Dr. Burrow's views, already put forward in a large number of publications, are concerned with the generic rather than the individual factors that make for neurosis and the objections to the modern conception of mental illness as social maladaptation. Although there is much labouring of commonplace observations and opinions in this book, it is valuable as offering an original method for the study of social psychology. Unfortunately the author is more occupied with formulating than with describing what he and his associates have actually done when observing " the discernible underlying physiological strains and tensions." Protocols and immediate observations, instead of so many abstract terms and discussions, would make the book more intelligible and useful.

THE SINGLE WOMAN AND HER EMOTIONAL PROBLEMS

Laura Hutton

(Baillière, Tindall and Cox, London. 1937. 2nd Edition. 5*s*.)

This simple booklet is intended to be read by single women who have given up any hope of marriage and by the friends, clergymen, and doctors who might be called upon to advise them about their emotional problems. It is almost entirely an apologia for close or homosexual relationships between these women. The exposition is neither sentimental nor original ; it is based on modified psychoanalytical theory. It cannot be said to have much to do with medicine.

THE MENTALLY ILL IN AMERICA

A History of their Care and Treatment from Colonial Times

Albert Deutsch

(Doubleday, Doran, New York. 1937. $3·00.)

There are so many links and parallels between psychiatry in Great Britain and in the United States that this admirable book does much to compensate for the lack of any corresponding work for this country. The author, not a psychiatrist but a social historian, has made himself remarkably familiar with the copious documents and problems relevant to his theme, and his sober, balanced account is an instructive piece of social as well as medical history. His incidental references and comments on English events, e.g. in the chapter on " Insanity and the Criminal Law," are excellent ; it is therefore remarkable that in his discussion of the sterilization of mental defectives he makes no allusion to the Brock Report.

DER SELBSTMORD (SUICIDE)

R. Weichbrodt

(S. Karger, Bâsle. 1937. Swiss frs. 19)

The literature of this subject is so great that a comprehensive and readable review, such as Professor Weichbrodt's, is welcome. Although there are rather more quotations from the poets than is usual in a monograph of this sort and much space is devoted to famous individuals who wrote about suicide or committed it, the statistical evidence and general problems are also examined, summarily and critically. The author is unwilling to concede to mental disorder the important part in the causation of suicide generally given it; it is unlikely, however, that his maximal estimate of 10 per cent. for the proportion of all suicides who are mentally disturbed is valid. He does not seem to distinguish sufficiently between abortive and fatal suicidal attempts.

MENTAL THERAPY

Louis S. Loudon

(Covici-Friede, New York. $12·50)

In two large volumes Dr. Loudon presents the case histories of 50 cases of psychoneuroses, perversions, and psychoses, after a preliminary section dealing quite briefly with the theory of psychoanalysis, the meaning of the dream, the psychopathology of the child and of the adult.

These cases are interesting especially, of course, to the psychoanalyst, but the ordinary reviewer is struck by certain points. In the first place the story is remarkably similar in all the cases so that he is reminded of a remark made by Bernard Hart many years ago, namely, that those subjected to psychoanalysis are rather like a series of bodies passed through a mangle, they all come out much the same shape. Further, they all tell very lurid tales not only of their sexual phantasies but of their actual sexual experiences. Is it that the instable personality has a much more eventful sexual life than others, or that the skilful analyst extracts a more truthful history than is usually possible, or that fact and phantasy are inextricably mixed in the patient's mind? While admittedly the accounts given of the analyses cannot for reasons of space be complete, it does appear that the interpretation of the dreams recorded is somewhat arbitrary and over uniform. There is no claim that the results of the analysis are always therapeutically effective, but in many cases the results would seem to have been very satisfactory, better in all probability than could be expected from any other method. A glossary is given at the end of the work.

The question that must be raised in respect of this, as of other similar books is, for whom are they written? For the convinced psychoanalysts it is one more series of clinical records of which many have already been published. It is assumed, however, that the book is also directed to the seeker after truth who does not belong to this group—otherwise why is a glossary necessary? It is very doubtful in the reviewer's opinion whether such individuals will be convinced or converted, but nevertheless the human documents here set out are worthy of the attention of all serious students even though they do not accept all the comments and conclusions of the author.

READING, WRITING, AND SPEECH PROBLEMS IN CHILDREN

A Presentation of Certain Types of Disorders in the Development of the Language Faculty

Samuel T. Orton

(Chapman and Hall, London. 1937. 10*s.* 6*d.*)

Unlike the three previous Salmon Memorial Lecturers, who dealt with the largest psychiatric issues, Professor Orton examines a limited topic, chiefly neurological and pedagogic in its implications. It is an epitome of the well-known work which he began in Iowa and continued in New York ; his debatable views on lateral cerebral localization and dominance do not, however, receive disproportionate emphasis here. The lectures are addressed not only to physicians but to teachers and parents, for whom a glossary is provided. Although the subject is so specialized, it is clearly presented, without excessive detail. In the first lecture aphasia and kindred disorders of adults are described, especially in their bearing on " laterality." The second lecture treats of disorders in the development of language in children, the hereditary factors in their causation, and the emotional and behaviour reactions associated with them. Problems of interpretation and treatment take up the third lecture, in which it is a little surprising not to find lengthier reference to the cognate difficulties with arithmetic which some children have.

THE BASIS OF CLINICAL NEUROLOGY

Samuel Brock

(Baillière, Tindall and Cox, London. 1937. 21*s.*)

The title of this book is somewhat misleading in that the book contains an account of the anatomical and physiological principles underlying clinical neurology. It is a readable survey of modern applied neuro-anatomy and physiology. The diagrams are excellent. It covers too wide a range for the ordinary medical student, but can be strongly recommended to those inclining toward a special study of neurology.

NEUROLOGY

Roy R. Grinker, M.D.

(Baillière, Tindall and Cox, London. 1937. 2nd Edition. 38*s.*)

It might reasonably be expected that a volume with this title, and comprising a thousand pages, would be an authoritative survey of the subject. That a second edition appears after four years shows that there is a demand for such a treatise. Nevertheless we feel that readers will be profoundly disappointed when they have occasion to refer to its pages.

The very foundation of neurology is clinical medicine. Upon the protean manifestations of nervous disease rests the whole structure. The description of the evolution of clinical neurological pictures is here minimal, and in its place is a symptom and sign analysis which is very scant, except for some major diseases. Further, particularly in respect of what may be called the minor syndromes, such as varieties of vertigo, facial spasm, the Brown-Séquard syndrome, the facial paralysis of syphilis, and a score of others, the description, brief as it is, is widely divergent from the everyday facts of the medical neurological clinic.

The author states that " the book is an attempt at a correlation of certain biological data which are considered of importance to the study of the human nervous system in health and disease." It is his belief that " in this manner an adequate instruction in neurology to students of medicine can be presented." Biological data are doubtless important in the discussion of pathogenesis of many disorders. In the practical issue the detail of the biological data becomes relatively slight to the neurologist in the clinic. To the investigator it must be exhaustive in his particular compartment. This account will not satisfy either.

The outlay of the book is admirably planned in that it leads gently from general anatomical, physiological, and then pathological considerations to detailed examination of the various organic nervous disorders. Each chapter is an essay on pathogenesis in which the most recent hypotheses are given the most prominence. It lacks the philosophical character and personal touch which would be necessary to avoid what might be called the year-book style, and the encyclopædic reduction of a mass of opinions and hypotheses gives none adequate treatment. Considered as a comprehensive but unsatisfying collection of views on this aspect of the subject, the work will obviously require frequent revision to be kept up to date.

NEURO-OPHTHALMOLOGY

R. Lindsay Rea

(William Heinemann (Medical Books), Ltd. 1938. 42*s*.)

Most clinicians will acknowledge that there is need for a book dealing with neuro-ophthalmology. It was therefore with pleasurable expectancy that the author's book was accepted for review, but to all disappointments come, and this is one. It hardly fulfils the purpose expected of it and as indicated by the author in his preface. Intended as a book to bridge the gap between neurology and ophthalmology, it carries out this task in a somewhat juvenile manner. Many of the descriptions of the changes to be found in the fundus are incomplete—for instance, in describing papillœdema no adequate description of the macular fan is given, nor of the changes in the retina around the disc. The pupillary changes associated with the name of Argyll-Robertson could well be amplified. On the neurological side, the descriptions of various diseases of the nervous system are too short in many places and in others deal with matter not appertaining to the subject, such as the pathological findings in post-encephalitic Parkinsonism. The discussion of field defects covers so little ground that cannot be found in the average text-book of medicine that the book does little to help the student except to add another book to the many from which in his innocence he has to make a choice. It is difficult to determine the usefulness of this book apart from a repository of quite good coloured drawings of the fundus.

THE CHEMISTRY OF THE BRAIN

J. H. Page, A.B. (Chem.), M.D.

(Baillière, Tindall and Cox, London. 34*s*.)

The author is probably right in stating that the chemistry and metabolism of the brain have been comparatively neglected, and he is to be congratulated on this attempt to summarize the existing information and suggest new problems for attack. Incidentally, the title of this book is just a little misleading in that much of it is devoted not so much to chemistry in the accepted sense of the word as to metabolism. After

a chapter on sterols and another on phosphatides, the metabolism of fatty acids, carbohydrates, and nitrogenous bodies are discussed. Gas exchanges, normal and pathological, are then reviewed and there are chapters on the enzymes, electrolytes, physical chemistry of the brain, etc. The last will probably be of interest to clinicians. The last chapter of 50 odd pages on oxidations in the brain is contributed by J. H. Quastel. A large number of original references are given throughout the text and a list of the more important review articles precedes each chapter. On the whole the book is clearly and simply written and will be of great use to research workers and advanced teachers. Few neurologists will have the necessary biochemical knowledge to appreciate it. There are some curious lacunæ in the subject matter. For instance, in the chapter on electrolytes rubidium, tin, and even rhenium are discussed, but sodium and potassium are hardly mentioned. There are some strange misprints throughout the text which might all have been eliminated by more careful proof-reading. In spite of these minor faults the book is to be recommended to anyone wishing to make a study of the brain or its metabolism.

DISEASES OF THE NERVOUS SYSTEM IN INFANCY, CHILDHOOD, AND ADOLESCENCE

Frank R. Ford

(Baillière, Tindall and Cox, London. 38*s*.)

This is a book which should find a place in the library of all neurologists and pediatricians. It is, however, too encyclopædic for the student or general practitioner. In it will be found an adequate description of most, though not all, clinical syndromes occurring in children suffering from an affliction of the nervous system. Divided into short descriptive sections, each is followed by an adequate bibliography from which a worker with especial interests may obtain a lead as to the literature. Illustrations are plentiful—some might be left out in future editions, as they are unnecessary and do not add to the descriptions. Further, they do not illustrate signs such as spasticity, though the legends of some indicate that this may be the intention of the author. The author has appended to many sections a short description of an actual case. It is doubtful if this is necessary, for if the matter in the text be adequate it should not be necessary to repeat it by the description of an actual case. A book containing so much, so well printed, so easy to read deserves success and a better index.

ILLUSTRATIONS OF REGIONAL ANATOMY

E. B. Jamieson

(E. and S. Livingstone, Edinburgh. 2nd Edition. 1937)

The fact that after a short time a new edition has become necessary is in itself sufficient evidence of the usefulness of this collection of excellent illustrations. The chief change of the edition is the introduction of more colour, which is certainly an improvement. One might wonder, however, whether a more systematic application of coloration would not make for greater clarity. The constant change in the colours used for the same type of structure and the choice of colours, for instance, red and blue for fibre tracts instead of their traditional usage for blood vessels, is somewhat disturbing. This might be a point worth while considering in a future edition.

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